Biology for Engineers and Other Non-Biologists
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Week- 04
Lecture - 19
Mendelian Genetics: Non-Mendelian inheritance

Welcome to the next lecture on Mendelian genetics. This will most likely be the last lecture on Mendelian genetics. We said that many diseases are genetically linked and to (ha) usefully analyse such disease inheritance we could use Mendelian principles. We showed some examples, we looked at some examples and then came to the situation of X linked disorders, the disorders that arise due to alleles that are inherited from X linked chromosomes. We saw how the inheritance patterns could be different from those predicted by Mendelian principles and (and) say that you could work out this example and we would start this lecture by solving this example.

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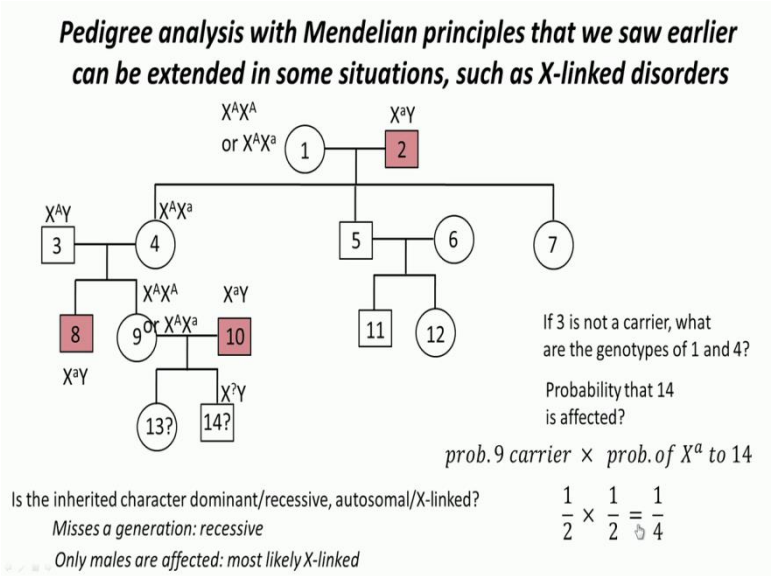

This is a (ped) a family tree parents and then the 3 offspring here, they marry and they have children and there is one more generation that is occurring here and after mating here, there are children here and we are trying to answer some questions related to these. The first question was; is the (in) inherited character dominant or recessive, is it autosomal or X linked; that is the first question. The second question was; if 3 is not a carrier as (gi) that is given (sam) probably the person has genotypic analysis (re) analysis results and (no) we know, we know that the 3 is not a carrier of the disease. If that is a case, what are the

genotypes of 1 and 4; that is the second question. The last question was that what is the probability that 14 is affected, okay?

So let us look at how to solve this. As you can see this disease misses a generation completely; 4, 5 and 7 (who) who are (ha) offspring of 1 and 2, is completely missed here, okay? If it is dominant, then this kind of a missing will not arise because one of the, as long as one of the genes is dominant the disorder will manifest. Therefore it is most likely recessive, right, since it has missed a generation that will happen only if it is a recessively inherited disorder and if you see here only males are affected, 2, 8 and 10 are affected, all are males and that will happen most likely if it is X linked, okay? Therefore it is a recessive disorder and it is most likely X linked.

Now let us try to answer this question; if 3 is not a carrier what are the genotypes of 1 and 4. We know that it is a recessively inherited disorder and most likely X linked so let us work it out. This person has to be X capital A, X capital A or a heterozygous person, X capital A, X small A, the person is not showing it is recessive there for even this kind of a genotype will not result in the disorder being manifest. And this is manifested here and it is X linked therefore this has to have a recessive allele on the X for it to be manifest in this male here, okay? So it is X small A Y here.

We are (the result) we are interested in 1 or 4 so far on this 1 could either be this or this is what we can say. Let us look at 8 here. This is an affected person therefore it has to be X affected male therefore there has to be a Y chromosome and it is X linked therefore the (X) the disease allele needs to be carried by X, X small A Y.

We know that this person is not a carrier therefore X capital AY, male and the (possible) this person is a female and not affected since it is a female it has to be XX. Since person is not affected and the father is affected this would be an X small A and the other one could should be an X capital A from the mother, okay, so that is the genotype of 4. So 1, we cannot say anything more than X capital A X capital A, X capital A X small A, it could be one of the 2 types whereas 4 be, can be or is X capital A X small A, okay, those (are) that is the answer to that question.

Now what is the probability that 14 is affected? 14 is here therefore we need to look at the parents here, this is a female, the mother is a (fe) female therefore its XX and the mother is not affected therefore either both capitals homozygous or capital small heterozygous in both

cases the person will not be affected. The father is affected and therefore it has to be X small A Y and therefore the probability that this male will be affected X what Y, the Y is coming from the father and what is their probability that this would be a X small A, that is what we are asking.

The probability that this will be an X small A depends on the probability that the mother is a carrier, okay? Therefore it is something like this; probability that the mother is a carrier times the (pro) probability that X a goes to 14 or this has become X a, the person as has inherited the Xa from the mother, okay? The probability that 9 is a carrier, see for example, if the mother is not a carrier then the mother is XAXA, right, X capital A X capital A, then 14 will not be affected at all, okay because Y comes from the father this Xa does not matter. So the Y will be affected only if the affected allele comes from the mother, this X small A. So it is the probability that 9 is a carrier and Xa goes to 14.

Probability that 9 is a carrier is half, okay these are the 2 possibilities and one of which is we are considering and the probability of X small A going to 14 when X capital A is also there, is another half and therefore the (probab) the probability that 14 will be affected, 14 will have genotype X small A Y is half into half, that is one fourth. So that is the answer to the question. I I am sure many of you have the right answer, you can check this.

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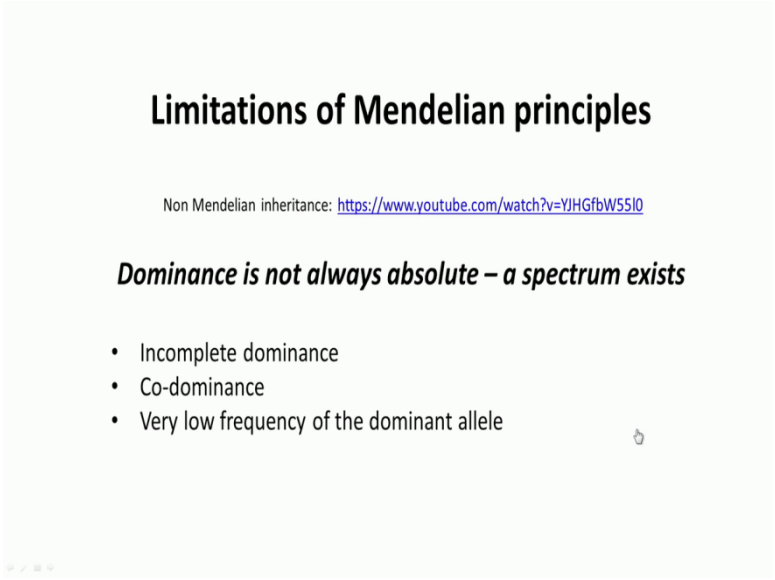

Let us finish up with what we said earlier the Mendelian principles as we know (ha) have limitations. We cannot apply it blindly to everything but we can apply it to large number of diseases that show Mendelian inheritance, okay? That was the use of learning Mendelian

principles. There are a lot of non-Mendelian inheritances, please check out the video that is given here. The first non-Mendelian principles that are going to look at is that dominance is not always, excuse me, absolute, a spectrum exists. It is not either purple flowers or white flowers, okay? There is something in between also that could arise. It does not happen in the pea plant but it happens in many other things.

That is called incomplete dominance or co-dominance is a variant of that and there could be very low frequency of the dominant allele that we have already seen. This is slightly different from what we expect. That is the reason why I have put it down as something that is different from expected. It does not go with the other 2. We have already seen this in the case of Huntington's disease, okay? The very low frequency of the dominant allele as long as you have the dominant allele you are going to get the disease, but the presence of the dominant allele itself has a very low frequency in the population, okay? So that is what this means. So this is not always absolute, a spectrum such as this exists from incomplete dominance or co-dominance to complete dominance.

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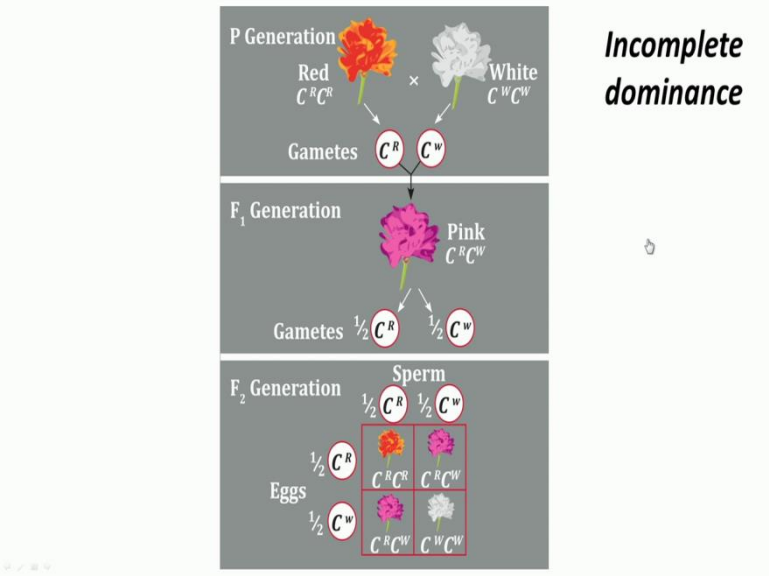

An example of incomplete dominance (is) is something like this in the case of a different plant. The, if you take true breeding red and white flowers and cross them together, the gametes will be capital R and capital W. In the F1 generation, all the flowers would be pink, somewhere in between red and white, okay? So it is neither red nor white, CR (C) C capital R, C capital W has resulted in a pink flower, no longer a red flower. And this is an example of incomplete dominance. You take this further, you have the gametes from the F1 generation is C capital R, C capital W, half and half and then if you do a panelled square analysis, one

fourth would be red, half would be pink and one fourth would be white in the F2 generation. This is an example of incomplete dominance (is) which is different from that predicted from Mendelian principles.

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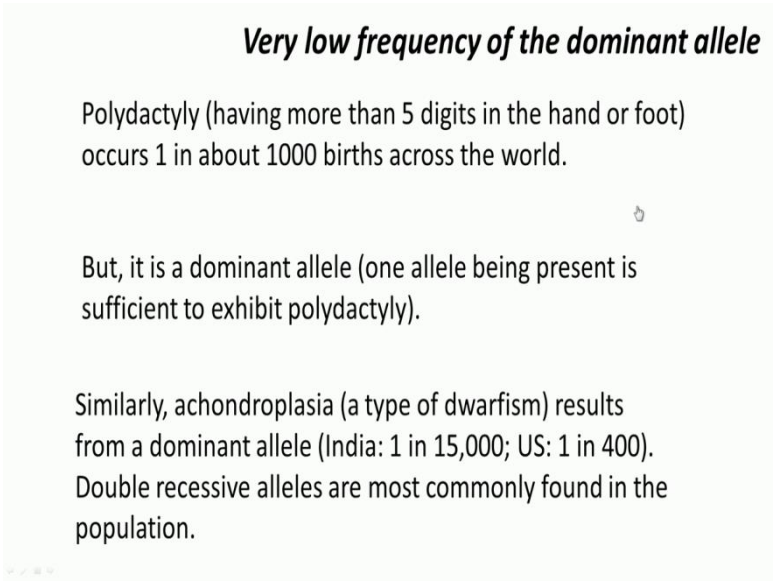

Very low frequency of the dominant allele, we have already seen the example, one more example is polydactyly, more than 5 digits in hand or a foot, okay? It occurs in about 1 in 1000 births across the world. It is the dominant allele, one allele being present is sufficient to exhibit polydactyly, but we know that a majority (is) are not (pali) polydactyl, right? So dominancy dominance does not mean a majority, not always. So that is something that we need to keep in mind.

Similarly achondroplasia, a type of dwarfism, results from a dominant allele again. In India, about 1 in 15,000 have this achondroplasia, in the US about 1 in 400 have achondroplasia. And double recessive alleles are most commonly found in the population because if one allele had been dominant the achondroplasia would have settled whereas we know that only 1 in 15,000, are have the disease which means most in the population do not have rather they have recessive alleles they have (de) they do not even have one of the dominant alleles. This is the very low frequency of the dominant allele. We have already seen an example of Huntington's disease earlier.

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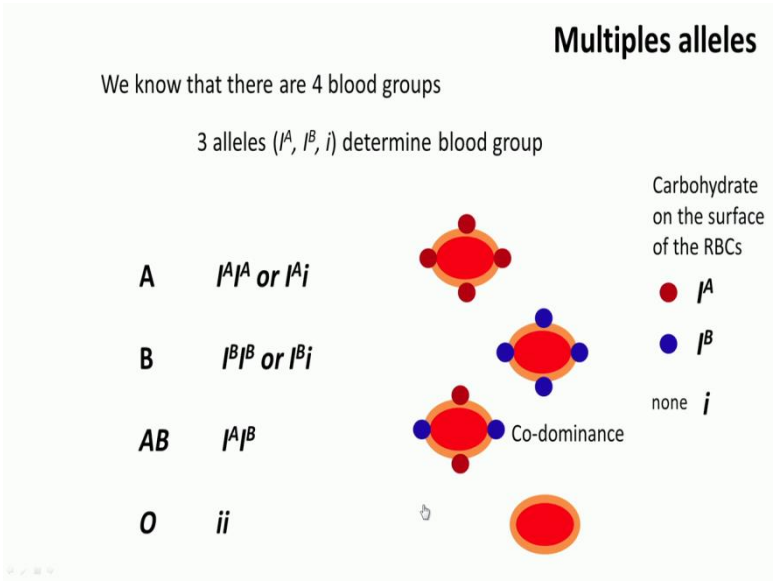

The next non-Mendelian aspect is that, multiple alleles can determine a trait. Okay, not just 2, multiple alleles. For example, it is a very good example that of blood groups, we all know. We know that there are 4 major blood groups, what, A, B, AB and O, right? And of course Rh positive, Rh negative, we will leave that aside for the time being. We know that there are A, B, AB and O and this is determined by 3 alleles, okay, 3 alleles, A (cap) capital A, capital B and nothing at all and written I, with a small I. I capital A, I capital B and small I, that we name it that way. These determine the blood group as for us.

The A type results, if it is either I capital A I capital A or I capital A small I, okay? If it is it is a B group, but is I capital B I capital B or I capital B small I, and if it is AB, if it is IA IB both

capitals and if it is O, when neither A nor B are present or in other words, small I small I. These are the alleles. In terms of what actually happens this A and B referred to carbohydrates on the surface of RBCs, A and B are different carbohydrates.

And I A or an A carbohydrate is represented by a maroon circle, a B carbohydrate by or a red circle, B carbohydrate by a blue circle and if there are no carbohydrates neither A nor B and it is small I. So if this is the red blood cell disc shaped red blood cell, if it has all A carbohydrates being expressed then it is blood group A. If it is all B carbohydrates being expressed, it is blood group B.

If it is both A and B carbohydrates being expressed it is AB and if none are present it is group O, okay? And this is also an example of what is called co-dominance were both A and B are expressed are shown are showing up simultaneously, okay? That is what is called co-dominance which is again a difference from the Mendelian inheritance.

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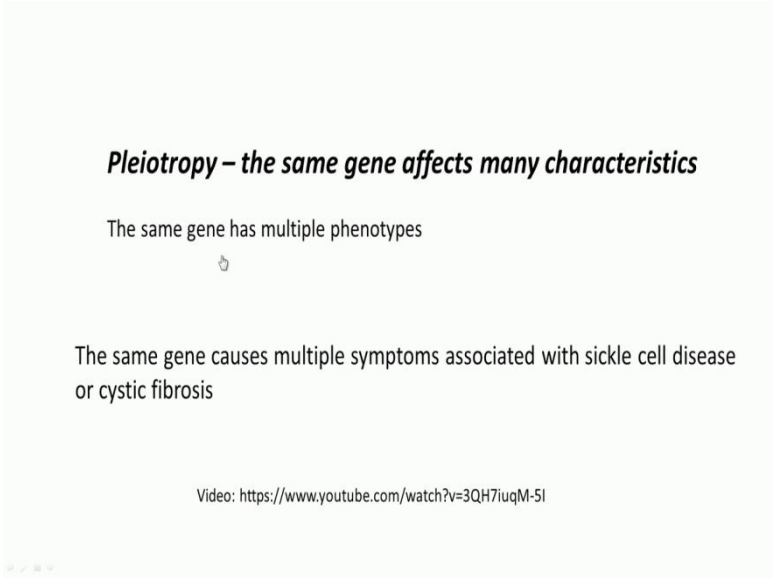

Pleiotropy is again Non-Mendelian. This means that the same gene affects many characters, not just one, it it affects multiple phenotypes. An example is from this the same gene causes symptoms associated with sickle cell disease as well as cystic fibrosis, okay? You can look at the video that is given here, the (p) last video that is shown that will give you some more details about Pleiotropy.

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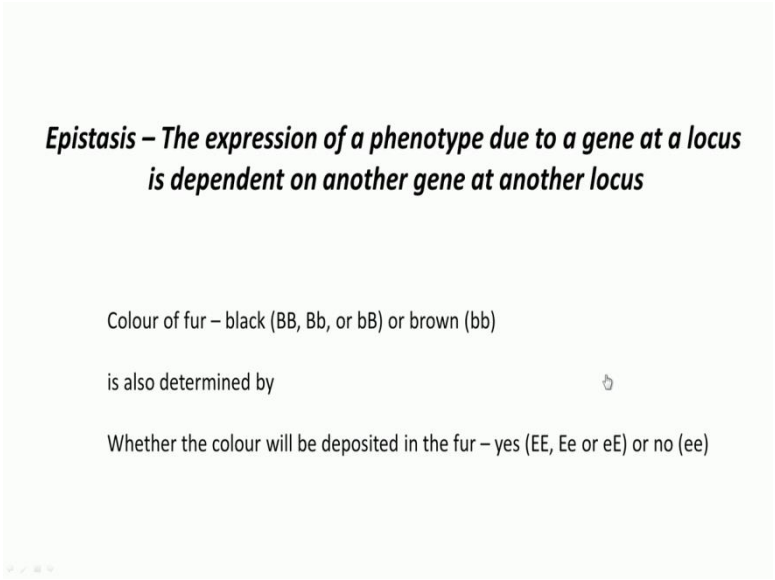

Epistasis which is the expression of a phenotype due to a gene at a locus, I mean epistasis arises when the expression of a (phen) phenotype due to a gene at a locus is dependent on another gene at another locus, okay? Expression of one is dependent (on) on the other. If that happens then it is called epistasis and again this is clearly non-Mendelian, this happens.

Example is the colour of fur it could either be black which arises from a dominant B, capital B or brown from a double recessive (s) small B. But, the colour of fur is determined whether the colour itself is expressed not, okay, whether the colour will be deposited in the fur or not. If it is deposited then again it is dominant, if it is not deposited it would be recessive, double recessive, homozygous recessive. So the not only what colour it is, whether the colour will be deposited in the fur, both determine whether the animal turns out to be black, the animal fur turns out to be black or brown or no colour at all, white, maybe.

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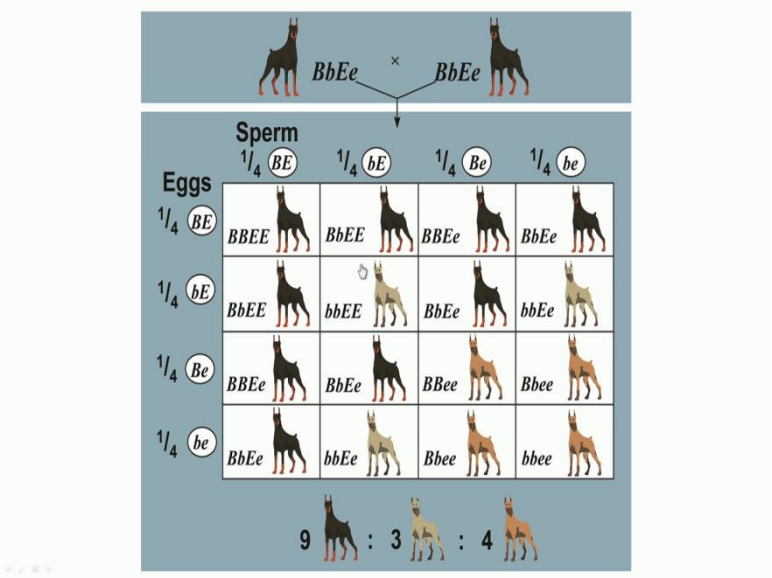

This is an example of such a cross, okay, in other words you could analyse this using a dihybrid kind of, dihybrid cross situation. If you do a dihybrid between colour and expression of that colour, okay, whether the (depos) whether the colour is deposited as shown by this E, then this kind of a panelled square results from these 2 characters for these 2 aspects, or these 2 characters and both those characters together determine whether the colour is seen ultimately in the dog or not.

For example in this case, 9 would have the colour, 3 will not have the colour, 9 would (have) 9 would be black, and 3 would not have the colour at all whereas 4 would be brown; the dominant, recessive and no colour at all, right? So this is different from the classic Mendelian panelled square, for 2 characteristics.

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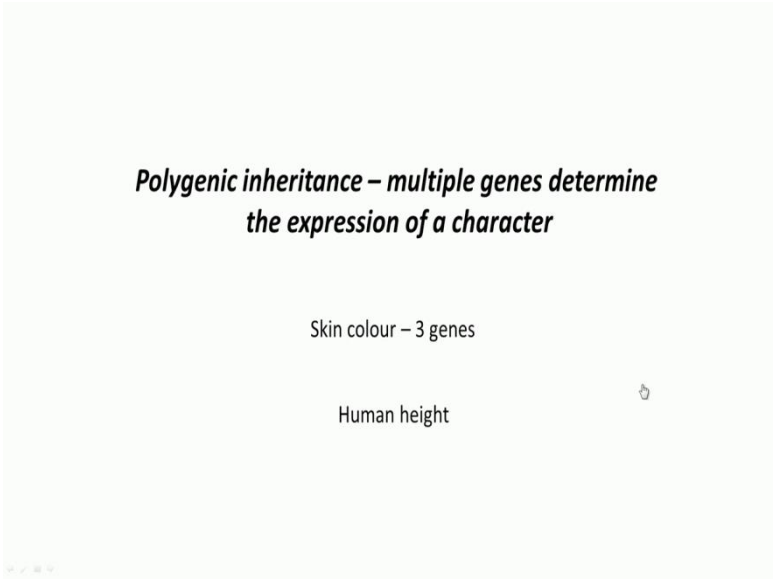

Polygenic inheritance is another variant again from Mendelian inheritance where multiple genes determine the expression of a character. The skin colour is determined by 3 genes. The human height is again a good example of polygenic inheritance where multiple genes determine the height of person. And therefore there is a smooth variation, there is a continuous variation in heights, in skin colour and so on so forth, because multiple genes are determining this, in the case of skin colour it is 3 genes.

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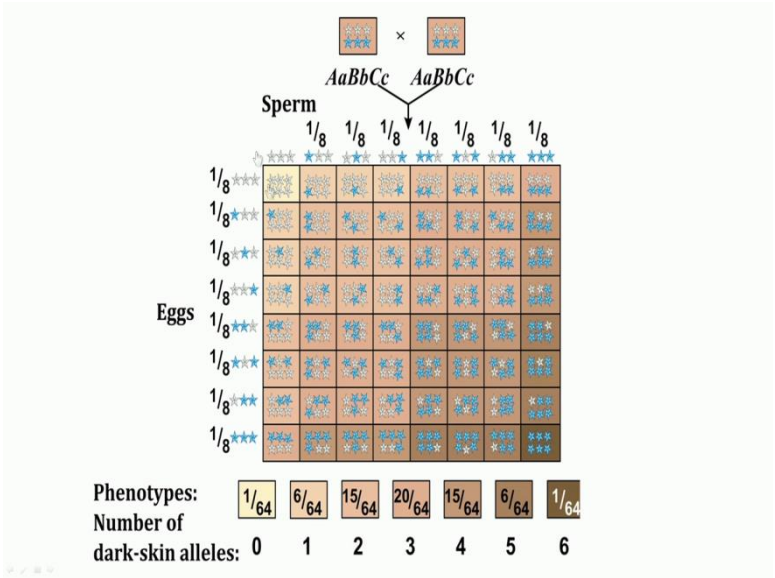

This is a panelled square it shows a tri-hybrid cross. As you could see at least 7 different possibilities exist, no colour at all when everything is recessive here and then 6 by 64 of this colour, 15 by 64 of a slightly darker shade, 20 by 64 of a darker shade, 15 by 64 of a darker

shade this can be obtained if you do, if you go through the various numbers of the blue, bluely shaded stars that are given here, that would directly show the intensity of the colour here and as you go along the intensity increases, 15 by 60 for higher intensity, 6 by 64 even higher and 1 by 60 the darkest, the darkest possible here that arises of all these 6 are of a certain kind, okay? So these are the various phenotypes, the number of dark skin alleles and so on and so forth were 3 different genes determine the skin colour.

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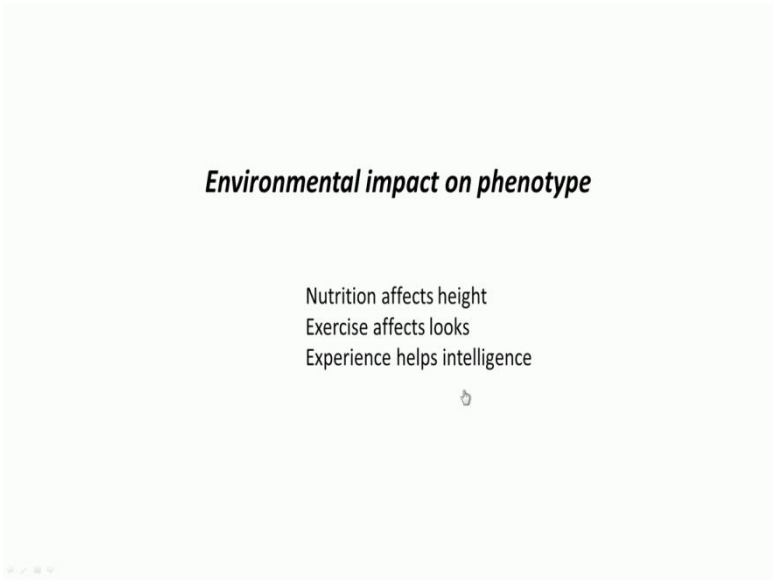

The last thing that we are going to see is that even the environment could have an impact on the phenotype, okay? Not just the gene, the environment in which the gene is expressed could have an impact. For example nutrition affects height. The height could be determined by a number of genes but whether the person grows up to the height potential, determines the nutrition, right? So the environment is determining the height. The exercise affects the looks, maybe you are born with the looks but you need to exercise to reach the potential in terms of the looks. Experience helps intelligence and so on.

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The (pic) pictorial example that I have here is the colour of a hydrangea flower. It could either be this colour or this colour depending on the acidity level of the soil, okay? Nothing else, it is a same gene, same expression and so on and so forth but which colour is expressed determined is determined by its environment and condition, in this case the soil acidity, okay?

I think that is good enough basal information in terms of whatever we looked at after an introduction, we looked at biomolecules, in terms of stories and so on, just to make sure, it is just not a set of information. We saw that there are 4 major biomolecules, carbohydrates, proteins or amino acids, whichever you want to call it. Then nucleic acids, lipids and each one has their own structure and the structure determines its function and so on and so forth; (the) that was the major take-home lesson from that particular set of lectures on biomolecules.

And we also looked at cell growth; why is it important to quantify cell growth; (in) by cell growth we mean the population growth, the number of cells or the mass of cells increasing, mass of cells per unit volume, number of cells per unit volume increasing with time, okay? How do you go about quantifying that you can do that using the first order relationship and how you could use that to find out the time for operation of a bioreactor, that also we saw?

And then some principles of Mendelian genetics the Mendelian genetics that we had developed a long time ago, it was given as a part of (an) of a basic course because although they were developed a long time ago they are simple enough to be easily used to predict the occurrence of certain genetic disorders. After that we saw some variations such as X linked

inheritance of disorders and the non-Mendelian inheritance characteristics, very many different kinds of those, okay?

You could look at this in association with what you pick up from Dr Madhulika Dixit's lectures, and that would give you some basis on the molecular aspects of biology which you could apply to your own requirements later, to address your own challenges later. At least you have been exposed to this, you know where to go and pick up more information more specific information as and when the need arises, okay?

One last thing, I would like to leave you with this thought to tell you the level of complexity that we are dealing with even in (understand) understanding the cell completely. Once we understand the cell completely then possibly the manipulations aspects can get more rigourous and we have come to a stage where you could manipulate life. But, to give you an idea of the complexity that is involved let me just show you this.

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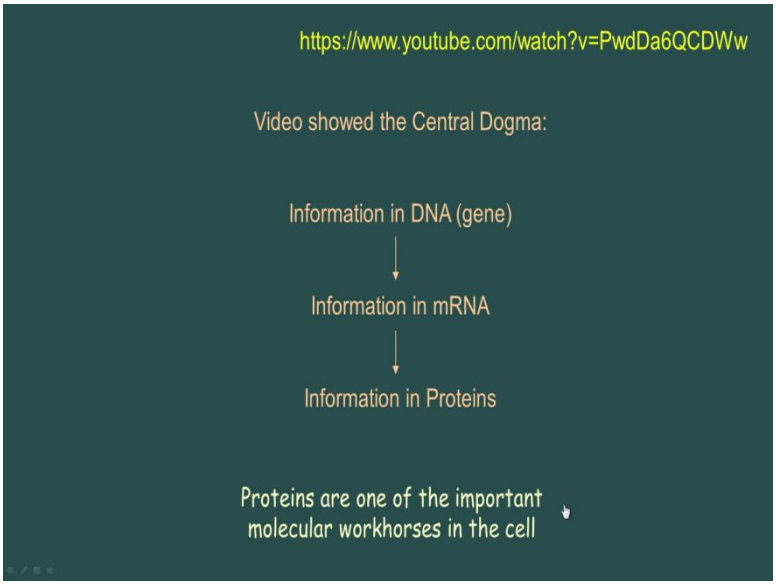

I am sure you (s) watched the video from nature publishing which was on the human genome project, which showed that the information in the DNA is transcribed to the information in the mRNA which gets translated to the information in the proteins, okay? And that is actually called the Central dogma, as you already know by now. And we are so interested in proteins because they are important molecular workhorses in the cell, they do lot of things in the cell each biomolecule is very important and there (this is), there could be more of a focus on proteins because it does so many things that are very apparent, that the basis of things that are very apparent, okay?

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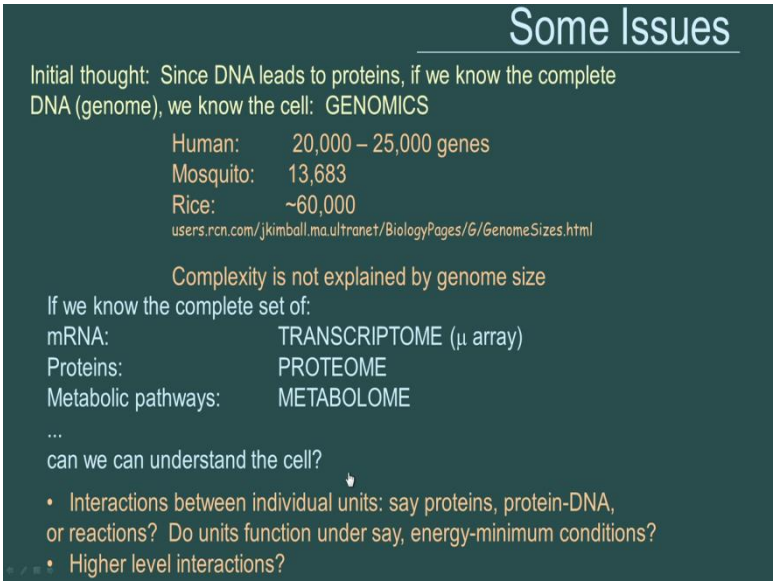

Let us look at some issues. When the DNA project, DNA sorry, when the human genome project was initiated the initial thought was, since DNA leads to proteins, if we know the complete DNA or the genome as it is called, we know the cell, okay? The source is Genomics view of the cell. If we know the blueprint we know the cell, okay, that was thinking and that was the motivation behind knowing the entire genome structure of humans which we came to know about 15 years ago.

However we were in for a lot of surprises. Humans had only 20 to 25 thousand genes, okay, that is from the site 20 to 25 thousand genes whereas even a pesky mosquito has about 13,683 genes, okay, not, not far apart from humans as we thought. And not just that rice has 60,000 genes. And there goes the concept of us being superior, right? (Ch) this has 3 times the number (of) approximately 3 times the number of genes that we do, okay, 2 and a half to 3 times, okay? So we can say that, if we assume that we are the most complex I, I am not very sure about that, but if we assume that we are the most complex we can say that the complexity is not explained by genome size, right?

Then people started thinking, if we know the complete set of m RNA, because DNA information goes to mRNA information (the) through transcription, so you know the complete mRNA information which is called the transcriptome which can be done through micro-array analysis and so on, then we know this cell, and if you know the complete set of proteins, the proteome, we know this cell.

If you know the complete set of metabolic reactions that the proteins catalyse through and so on so forth, we know the cell because there are so many interactions that are taking place and so on. And this can go on and on, okay, the (in) level of interactions between these various kinds, are so many. So when can we understand the cell really? That is the question, you do not really know.

Also interactions between individual units, say proteins, amongst proteins itself is 1; protein-DNA, okay, or protein-something else or maybe carbohydrate-something else and so on or reactions that (oc) that occur in the cell. And do these units function under energy minimum conditions unlikely, right? And are there higher level interactions, ya definitely there are and how do you go about understanding this.

And as we speak people are working on all these things. Hopefully sometime in the future we will have a better understanding of the cell and therefore a better understanding of life itself. Hope that you enjoyed this course (and) there will be a few more lectures that come up in terms of, which takes, or which throws light on some of these aspects such as DNA, the processes related to DNA and so on. Wish you had fun. Bye.