Introduction to Cell Biology
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Introduction to Genetics – Part 3

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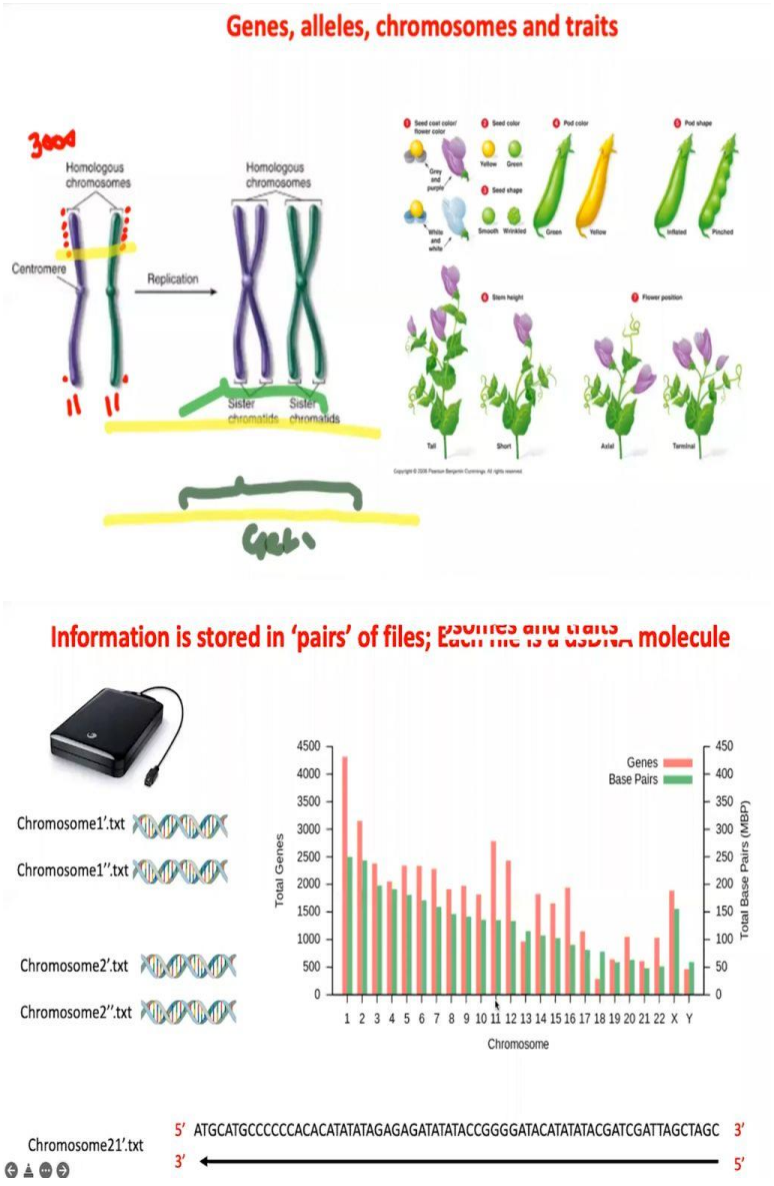

So, in a diploid organism, so here is your, here I have homologous chromosomes over here. They are genes all across the length of this chromosome. And if we take any chromosome from here, chromosome 11, chromosome 11 is 3000 genes. So, if this is chromosome 11, homologous chromosomes one comes from mother, one come from father. This chromosome will have 3000

genes. And if we label them from one end to the other, gene one will be here, gene two will be here, gene 3, gene 4, gene 5, gene 6 all the way till gene 3000.

The same genes are also in the homologous chromosome, all the way to 3000. You will have in this location over here, the same gene in both the chromosomes. So basically, we have two copies of the same gene in these homologous chromosomes, which are in the nucleus and which are inside the cell in our bodies.

Now, if these two copies are can be identical or can be different either way, they are alleles of the same gene. So for a diploid organism, which has two homologous chromosomes, there will be one gene because the information is the same; but there will be two copies, and the copies are called alleles. Is that clear?

Student: So, means gene is a fundamental of a, like a fundamental part of a chromosome and allele is a group of that gene.

Professor: No, I would not put it like that. I would say that in a single stretch of DNA which is here, there is a physical region; we have talked about this, where there is a locus which we defined as a gene, which is transcribed and translated. All I am trying to tell you is the homologous chromosome will have exactly the same information; and it will have the same gene in the same location, which is pretty much over here. And these two copies are called alleles.

Student: Ok sir, got it, thank you.

Student: Sir, in the next slide when you said unit factors, was that meaning alleles or genes?

Professor: So, here is where I am not trying to call.

Student: Sir, next.

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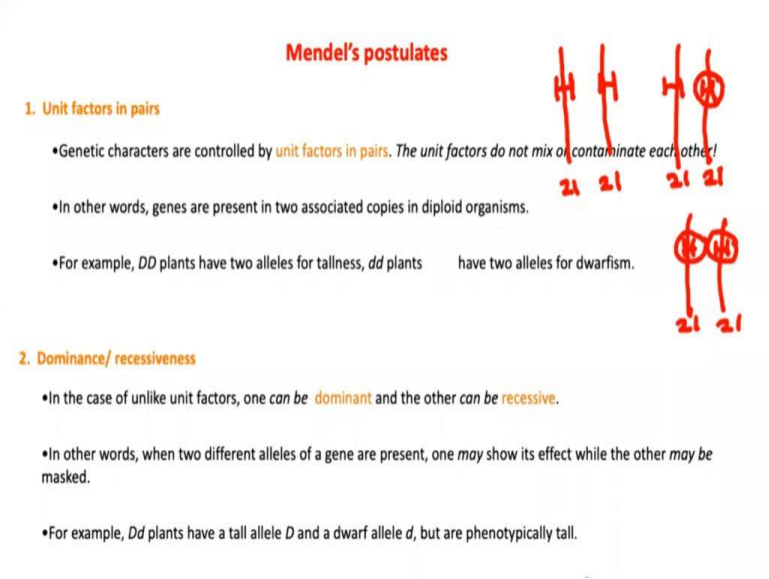

Professor: The moment you talk in pairs, the pair is there. There are basically the same; it is the same information; so it is the same gene. When you say there is a gene for hemophilia; if there was a single gene for hemophilia, which there is not. You are talking about a single pair of alleles, so its nomenclature.

Student: Please repeat your voice broke in between.

Professor: So, what I am trying to say is, let us say that there is a gene for which causes the disease hemophilia; mutation in the gene causes the disease hemophilia. There are many genes which do that; but for the moment, let us just call it a single gene. And let us say that the gene is called H. And this gene H will have two alleles in your body; because you are a diploid organism; so, there will be H and H. And one H will be on one chromosome, the other H will be on the other chromosome; and this might be chromosome 21. I do not know exactly where the hemophilia gene is.

Now, this is what we call it as a wild type gene. If the gene gets mutated, then you will have; let us say only one copy gets mutated. Then, you will have two H's; but one H will be have slightly different bases than the other H. So, we call this a, we say one copy is mutant. If both copies of the gene are mutant, then we will say both copies of the gene are mutant; but, their location does not change. And the fact that they are two copies of the same gene does not change. Clear?

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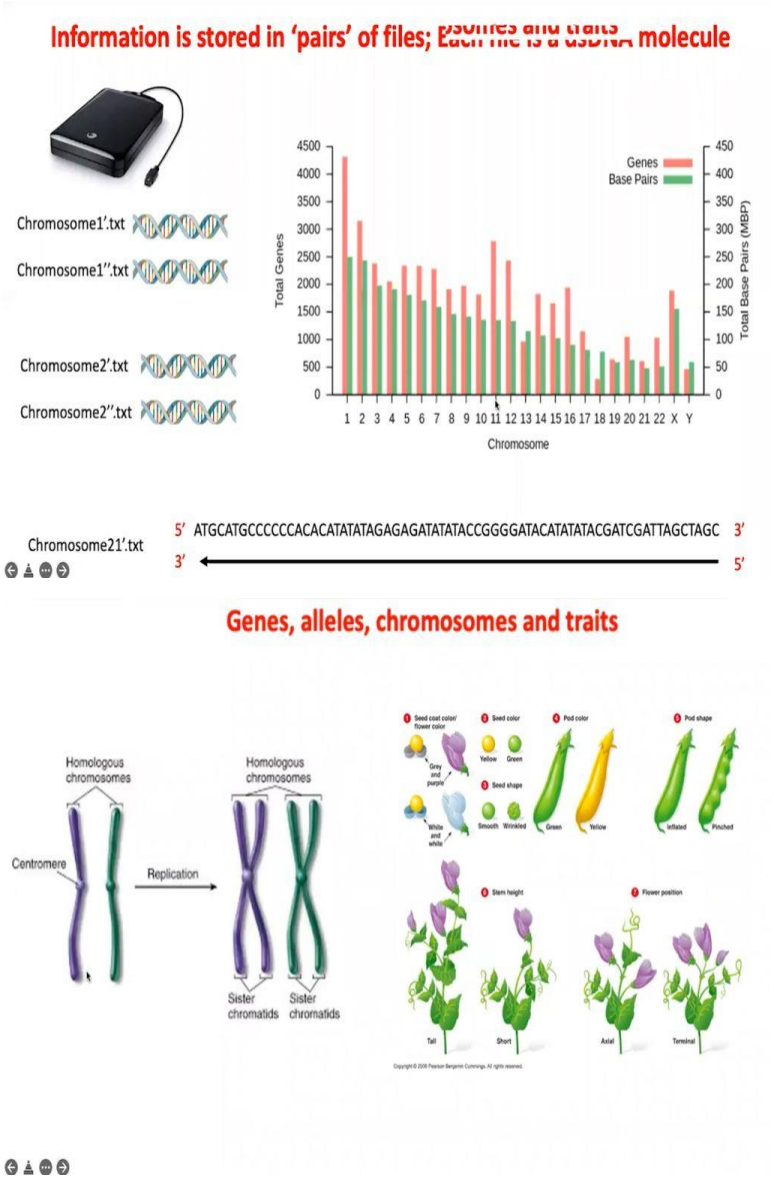

Student: Sir, can you please repeat what the inference we drew from the computer analogy of the genes, the hard drive one.

Professor: So, the analogy is only that I want you to imagine that. So, what I am trying to tell you is that all the information, which I am using right now to speak to you, for example, is because of information which is coded in the genome of my body. My muscles are moving, my vocal cords are moving, I am breathing. All this is controlled by finally by the sequence of nucleotides in our genomes.

So, this sequence of nucleotides in our genomes is on a entity called as DNA. It is a double helix, it is just ATGC ATGC repeated all over again. You can actually type it out as English text. And if you typed it out as English text, because the information is the same; it is just chemical in your body and typing. But the content is the same, is basically packaged in distinct chromosomes.

So, this entire long, let us say 400 MBP strand is chromosome1; and it is at its chemical nature, it is a double helix. So, each strand has this information and the second strand is complementary to it. And this is one chromosome, this one long strand of DNA. There is you have a redundant second copy in your genome because you are a diploid organism; so there are two copies on your genome of the chromosome.

Because they are two copies at any stretch, whatever if there is a gene coded by the stretch, the other chromosomes will have exactly the same gene coded in that stretch. So, the analogy is that these text files are nothing but information files and chromosomes are nothing but basically, packets of information, which. If you have 21 chromosomes, instead of having one large file with all the information, you have 21 files in your body; that is all the analogy is.

Student: Got it sir. Thank you.

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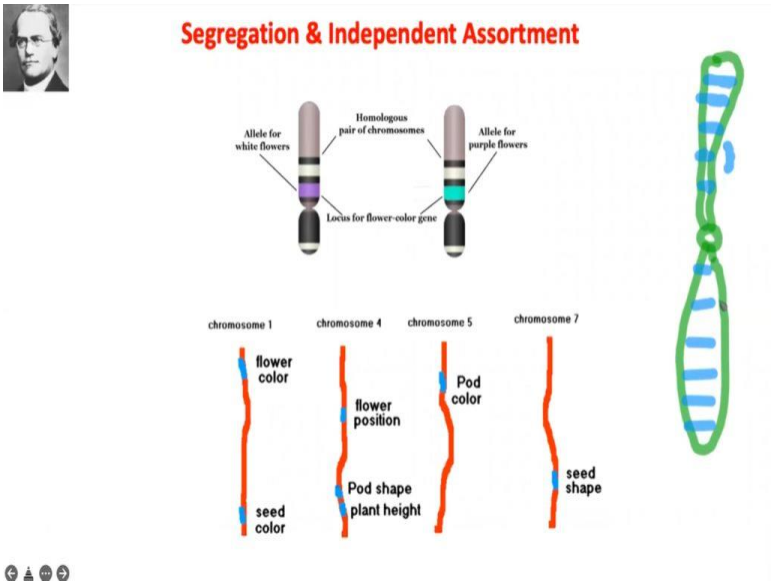

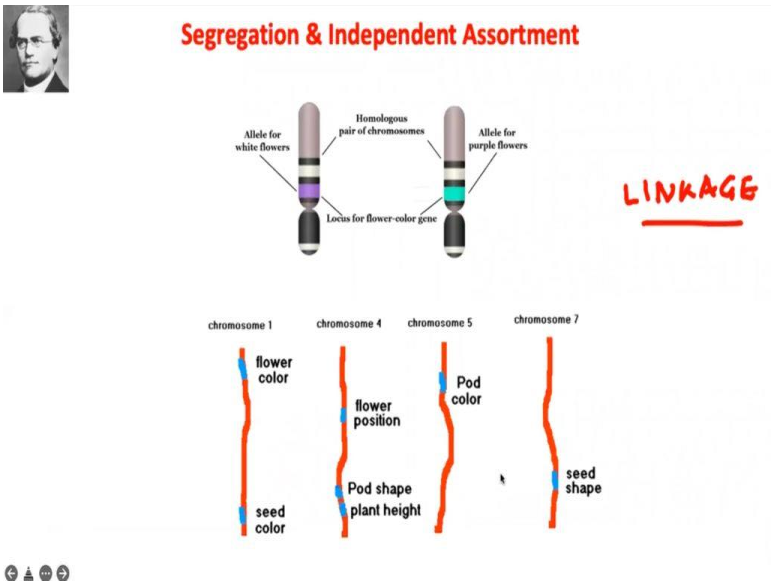

Student: Sir, what does this chromosome coloration indicate?

Professor: The red coloration?

Student: No, in the top, the top image where it is written homologous pair of chromosomes and all.

Professor: Right, when the early cytologists first saw chromosomes; they were not easy to see. It was only in the 1910s, 20s or 30s, that people started seeing chromosomes; making chromosomal preps was very very difficult. And one of the examples is the fruit fly Drosophila melanogaster, which is the organism I do research on. And one of the things they saw in certain unusually large chromosomes was that if you stained it with a variety of stains; what would end up happening is you would see, you would see banding patterns on these chromosomes.

So, you use stain one, you will see one banding pattern. You see another stain, you see another banding pattern and so on and so forth. So, this is just a schematic representation of the fact that there were banding patterns. This band is basically area of the chromosome which is nothing but a single double stranded DNA, which contains let us say 10 genes; because chromosome is large. They are let us say 3000 genes on this chromosome.

So, even this small stretch over here, which is showing a banding pattern or a staining will contain 20, 30, 40 genes. So, this is we know that they are banding patterns when we stain

chromosomes; the reason for this banding patterns is not particularly important right now. Any other question?

Student: Sir, is independent assortment only defined for genes or chromosomes?

Professor: The moment that if you are working with flower position and pod shape simultaneously; you have a problem, because they will not assort independently. So, one of the major concepts in genetics is the concept of linkage. What linkage basically means I am simplifying it is that any gene on a single chromosome is physically associated with all genes on that chromosome; and with exceptions, which you will study about in genetics like crossing over. These genes traveled as a group, so they are linked together. So, the moment they are linked together, they will not show independent assortment.

So, Mendel's rules will only work if you take one phenotype or one seed shape from one chromosome and pod color on another chromosome. So, his famous dihybrid crosses will always be from two different chromosomes. He did not know that, but that is how we are interpreting them today. So, I assume you understand now from a modern perspective.

Student: Sir, I have a very trivial doubt; during a reproduction. One set of chromosomes come from father side and one set that comes from other side. So sir, does that mean that information gets doubled at each generation or does that mean that half of the information is lost during the replication? I am during cell cycles or something.

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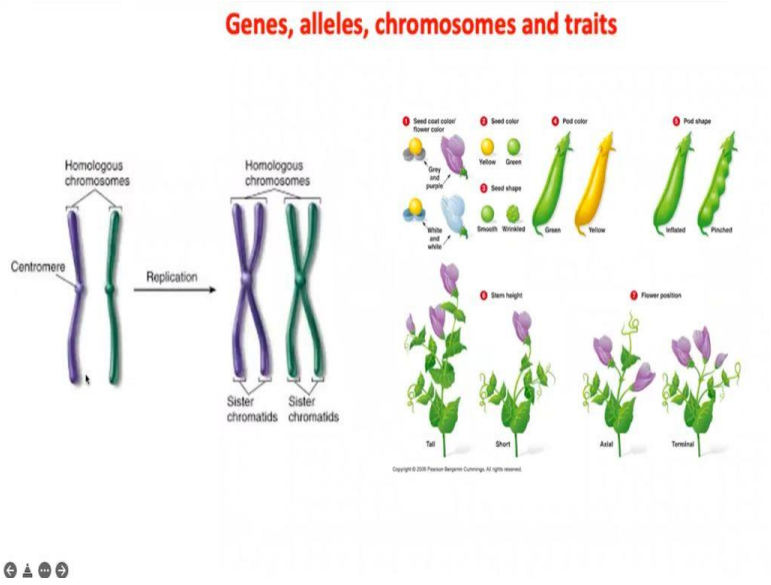

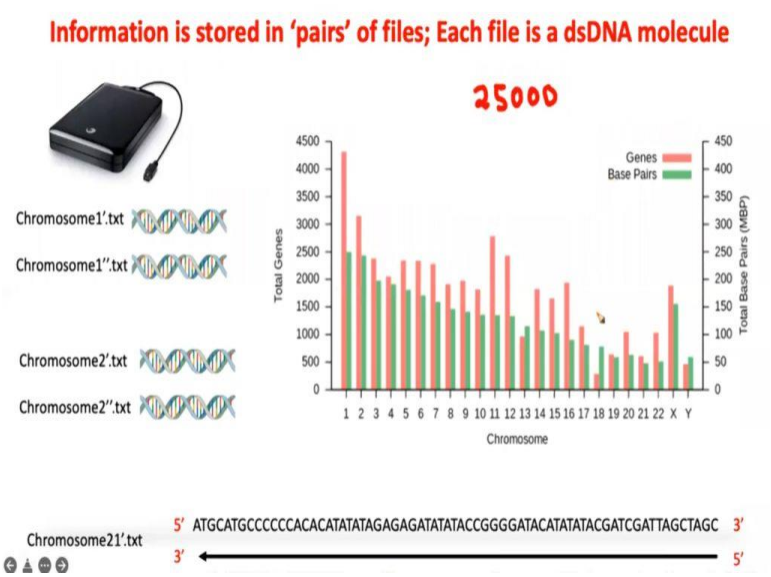

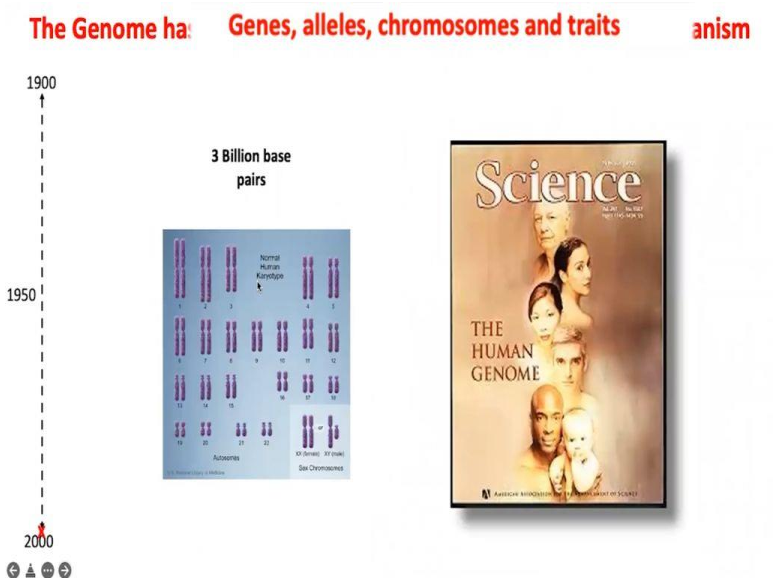

Professor: So, you have to remember that each chromosome if you take one of these homologous chromosomes; if it is one of the 21 sets, which you need to make a human being, one is enough. That is the reality; there is no law which says that you need both homologous chromosomes to make an organism. They are diploid organisms, they are haploid organisms; we are a diploid organism.

So, we have a double copy of chromosomes; one from mother, one from father with pretty much the same information. If one gene is different from the other; then, we say that the two alleles are not the same, they are different. So, for whatever reason, the way evolution has decided our fitness, it seems that it is better for us to have two copies of the same chromosome; one from the father and one from the mother.

But, that is not true in animal life, in or plant life. There are plants which have tetraploid; they are plants, which have 16 copies of chromosomes. There are animals microbes out there which survive on a single copy of a chromosome. So, what I am trying to tell you is we have two sets of information; in theory we can do with one, is that clear?

Student: Can we say that a chromosome has like some number of genes, and each gene has some different character?

Professor: In fact, that is the whole point. If you look at this graph over here, the humans have approximately though it is still controversial. And if the number is reasonably accurate now, humans have let us say approximately 25,000 genes. Now, each gene is has a different sequence

and it has different information. And that information is transferred through transcription to RNA, and RNA maybe a functional entity, or mRNA. Then mRNA makes a protein and the protein is a functional entity.

So, effectively every game is pretty much different. There are exceptions; there are duplicated genes, which do almost similar work. But, in general let us say out of 25000 genes, 23000 are doing completely different functions. Did that answer your question?

Student: Yes sir, thank you.

Student: Sir, I had a small doubt in the chromosome diagram. Sir, in this slide, the chromosome contained two chromatids; but in left side of diagram, they said a single chromatid as a chromosome.

Professor: See, this is a chromosome. This happens only during DNA replication, just before the cell is going to divide.

Student: In, for saying that they are homologous chromosomes, there should be two chromatids at least; so how they consider single chromatid as chromosome.

Professor: Who said? So, this is a chromosome. If it duplicates while it duplicates, it is still attached through the centromere; and we call each as a chromatid. I am not sure what the confusion is. If you look at the human karyotype over here, this is a karyotype. It is a actual picture of the way human chromosomes look. You can see that there are two homologous chromosomes over here. I think there is something with the schematic which is confusing you; maybe will get back to that. Are there any other questions?

Student: In that graph between chromosome and number of genes; the number of genes is exceeding the number of base pairs. So, does that mean that some of genes are overlapping in their code?

Professor: no, no it is not exceeding; this you have to is this kind of graph is something you do not see at all times that two axis.

Student: ok, ok I got.

Professor: a situation where that one axis shows a different.

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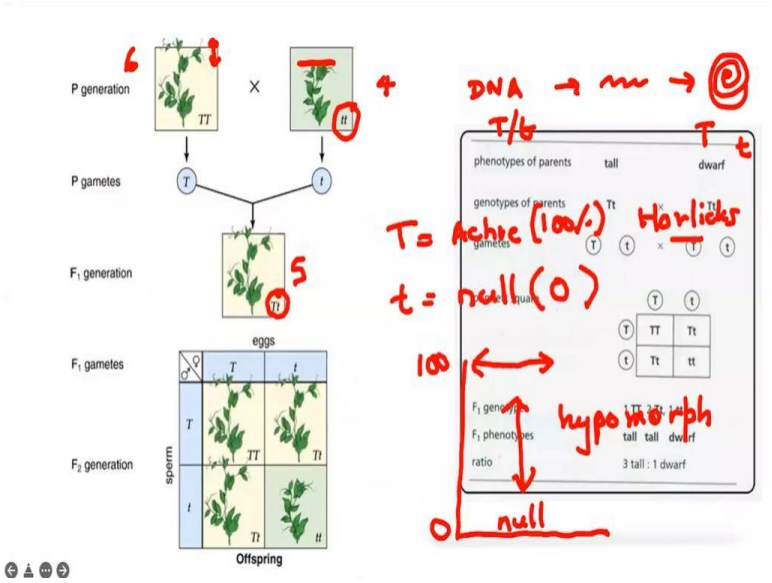

The point I want to focus on before I end this class is this idea of dominance. Now, all of you know that genes, there is a location on a DNA which is called as a T gene. The alleles are T or t. This DNA makes mRNA; this mRNA makes a protein; and the protein is now made from either T allele or it is made from a small t allele. Now, can you think of a reason why Tt combination does not give you any dwarf plants, and why why it gives you only tall plants? Can you reply?

Student: A protein which is formed from small t, it maybe ineffective or maybe deformed in some way; but the protein from capital T is much more functional.

Professor: So, let us take your example and I will say T makes a active protein; this is the simplest example. And T is a gene which is I am going to use the term null, which is a genetic term; which basically means there is 0 activity; and assign the capital T as 100 percent activity. So, now what is happening is the capital T which is active makes; I am again, do not take me seriously. I am just saying it makes Horlicks; and this is just to give an analogy, that it gives some growth factor, which causes this plant to become taller than average.

So, one copy of this Horlicks is enough, you get a tall plant. If you have a single copy, instead of having two copies, you still get the same height of the tall plant. You do not get an intermediate size. However, the moment you get two alleles which are not functional, you will not get a plant which is higher than a certain level.

So, let us say, call this 6 feet, this is 4 feet. So, you either get 4 feet or you get 6 feet; even if you have a single functional allele, you get 6 feet. The genetic term for this is haplo-sufficient, which means that to reach the maximum height possible, a single active T allele is fine.

So, the simplest explanation, molecular explanation for the Mendelian cross of Gregor Mendel, which has been reproduced many times is that the small t is a dysfunctional allele; it does not give the growth factor. The big T is a functional allele; it gives a growth factor. However, a single copy is enough to reach the tallest plant; and when this growth factor is completely missing, you get a dwarf plant. Does everybody understand this explanation?

Student: Sir, I have a doubt. If we say that T is like producing like 100 percent of say Horlicks; it is like double t should produce like 200 percent that we like more than t chromatid.

Professor: So, that is not happening over here.

Student: Why does that not happen?

Professor: So, one of the realities of genetics that so for example, if you are talking of growth factor. If the growth factor needs to bind to a receptor; I am using modern language. And that receptor has to signal to make, let us say more cells or give more height; you have reached a threshold beyond which you are not going to get any tall. And it turns out that a single copy of T of that allele of that gene is more than enough to make you reach that height. Beyond that, being excess is not going to make any difference; this is the way the genes are interacting in the P plant.

Student: like this is due to feedback inhibition of sorts that.

Professor: It maybe feedback inhibition, but the simplest explanation is beyond the point, giving more Horlicks level. And not only that, you are not seeing any intermediate stage.

Student: yes.

Professor: So, if you could have seen a 5 feet plant over here.

Student: yes, understood.

Professor: it would be additive the way you are suggesting it is; but, we do not. So, this is the way Mendelian discrete genetics is.

Student: Sir, tall plant will get better sunlight, so it wants to grow tall; so T is, capital T is dominating?

Professor: No. So, you see you are coming up with an explanation, which in this particular case has been already discarded; it turns out that this is purely a genetic phenomenon. This, is of course, sunlight is important; of course, nutrition is important. But, that is not all this is done under equivalent conditions of sunlight and nutrition.

Student: How did Mendel make sure that in the first case he has two capital T's?

Professor: By having pure lines; so that is something you have to remember very clearly, in your mind. Every experiment of Mendel was started with pure lines, which for generations bred true. So, if you cross a red cow to a black cow for example, to see what happens.

For the 10 generations before, red cow versus red cow mating only gave you a red cows. In this case, tall plant versus tall plant mating only gave him tall plants. And he covered these plants, let us say with plastic bags, and he kept them in a separate corner of his field; so that there was no chance of any pollen coming from a short plant and contaminating his culture. In genetics, you have to define your define the potential alleles in your crosses before you start your crosses; otherwise, things become very confusing.

Student: Sir, can we say that the small t allele is not transcribed at all?

Professor: is not transparent.

Student: no transcribe, transcription does not happen.

Professor: which is what I am saying; it is a null. It can be either not transcribed, or the mRNA may get degraded; or the protein maybe made, but it is not folded properly. So, in genetics, we say that every allele has let us just put a graph. This is where single allele functions which is at 100; and at 0 is what we call as a null. And anything in between, we use the term hypomorph; this is just terminologies, this is a important concept.

What I have tried to do today is to define Mendelian genetics in modern terms. For those of you who already know all of this, refresh your mind in terms of genes alleles, basic monohybrid Mendelian crosses. For those of you who are dealing with these concepts a fresh; you have to sit down and think, they are not as simple as it as they seem. Mendel's ideas of segregation is

basically alleles of two homologous chromosomes, on two homologous chromosomes separating. Mendel's ideas of independent assortment have to do with the fact that genes are on different chromosomes; and they do not influence each other, they are independent.

And the third one, which is of dominance is basically a concept of the fact that when they are two alleles, and one allele is mutant; in this case, we are taking the simplest example of a completely loss of function, null allele.

Then, you basically do not see it in the first generation. And it comes back in the second generation simply because two alleles and the laws of mathematics dictate that you will get the two null alleles back together in a ratio of 1 is to 3.