Introduction To Cell Biology
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Introduction To Genetics - Part 1

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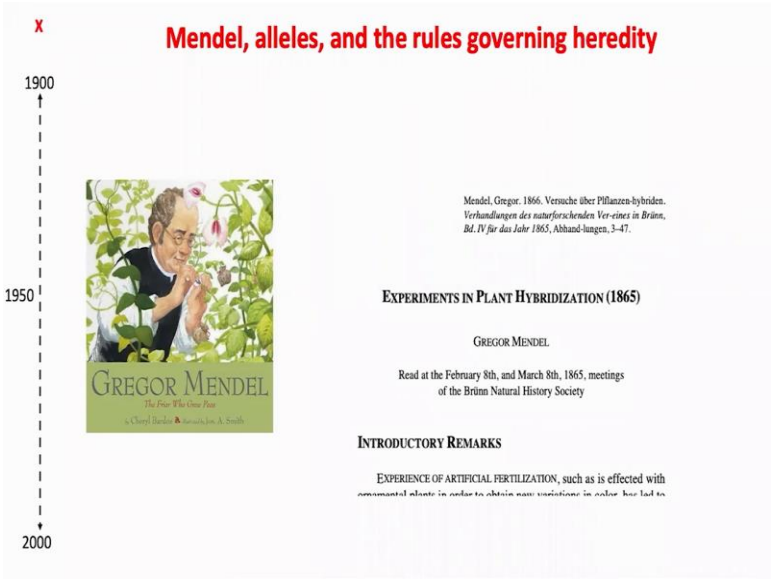

So, let me go to the module relates to Mendel's alleles, genes and generic ideas about heredity in terms of Mendelian genetics. Now, I know most of you have, at some time or the other at different levels, looked at Mendelian genetics. And what I will try and do today is, talk to you about Mendelian genetics that is true, but try and give a little bit more of a modern flavor. And what I am trying going to be doing is basically talking mostly about the modern view of genes, alleles and explaining Mendelian ideas using all the modern ideas. So, it is a little bit of a bottom up approach rather than the usual Mendelian approach.

And hopefully, that for those of you who have done this many times before, that will give you a little bit of new insight into genes and genetics. The goal, of course, is to introduce you to genetics.

So, as many of you know, Gregor Mendel was a reverend priest, who was employed in a monastery in Austria, which is currently that area as in Czechoslovakia. And he was a naturalist. He was trained in physics, Maths, he was a teacher used to teach mostly physics and as a naturalist he had varied interests, including astronomy.

And one of his interests was looking at what we call plant hybridization, and basically hybridization in the word, where it is used not in terms of DNA, but in terms of crossing animals and plants together is to bring together different characteristics of plant life or animal life to produce different combinations, which are more useful, for example, to mankind.

So, much of the wheat, the rice we eat today is basically taking wild varieties crossing them again and again and again, till you get rice, which is the kind of modern rice which we see today, better yield, better taste, all that has come about by 100s and 1000s of years of hybridization. Similarly, for animals, cows, as an example, the farmers for many, many years have been crossing different varieties of cows to get healthy cows, which give a lot of milk and which can be handled without any problems.

So, Mendel was interested in hybridization, his initial experiments were, with mice. And then he moved on to the pea plant, which is shown over here. And for a couple of decades, for a fairly large period of time, till he became the Abbott of his monastery, he did his own experiments, in a, I think, a couple of acres of a field behind the monastery where he did many of his experiments, as many of you know, his experiments are published in a German journal called experiments in plant hybridization.

This is, of course, the translation original language is German, in the year 1865-1866. And before this, he had presented his work at the local cities Natural History Society. And his work was barely cited multiple reasons he was from a small place. He was not a well known naturalist he was just a teacher and a monk in a monastery, he sent his work, published work too few people, and they probably did not understand the implications of what he was showing.

Because you have to understand that hybridization plant hybridization was a very routine thing done by many, many nationalists, Charles Darwin himself, did many more complicated and much more wider range of experiments with both plant and animal hybridization. So, it was not, the experiment itself did not seem novel enough. And his observations seemed a little odd. But again, it did not seem novel enough.

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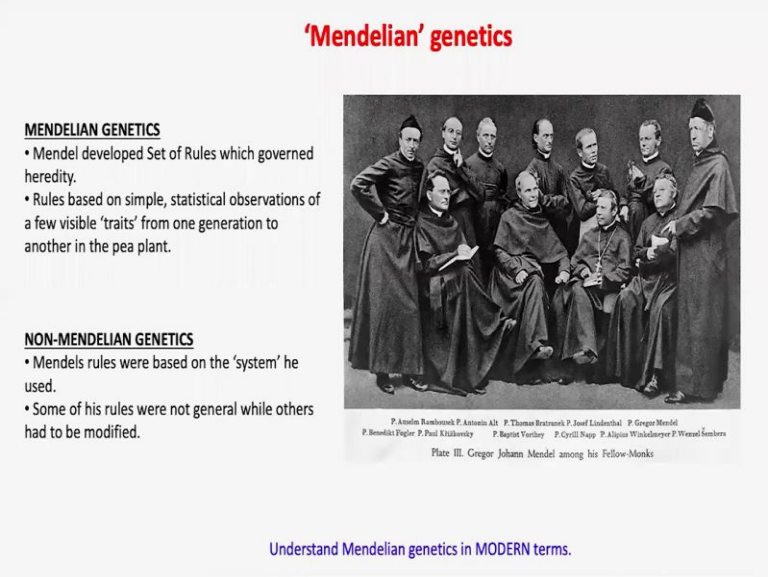

It was only sometime in the year 1900, where three researchers basically rediscovered his paper, conducted some of the experiments and came up with the idea that Mendelian and Mendel had, of course, passed away by the time he had passed away somewhere in 1880 or so. So, it took almost a couple of decades after his death to find his papers, and they realize that much of what you were saying was true. And they also realize the implications of the things he was saying.

So, what the Mendelian paper which is pretty much all that exists because much of his documentation was lost after his death, basically developed a set of rules which govern heredity. Now, they do not govern all of heredity. Heredity, as we realize today is much more complicated than simple Mendelian genetic. Mendelian genetics was all that was coherent in the years from 1910-1920 but today, we realize that genetics is a very broad area. And the rules of genetics are large and complex. But Mendelian genetics still found a simple, straightforward bedrock.

And if not, the actual laws of genetics, at least the definitions, which he came up with the idea of contour characters, rather than mixing of characters, the idea of traits, the idea of two different independent alleles, all these ideas are still very important that which is why he is revered as the father of genetics today. Now, much of what he did was setting up crosses with the pea plant, and looking at the phenotypes of what he could observe the changes in the color of the pea changes in the shape of the pea pod, all these observations he noted down.

And he saw some relationships. And these relationships, pretty much were used to what are called the so called laws of Mendelian inheritance. But they were actually just sort of thumb rules, which he came up with observations which were consistent, and seem to make sense, and were reproducible, at least in his experiments. So, what we will do in this class is we will try and understand Mendelian terminology, Mendelian genetics in modern terms, which is pretty much the goal.

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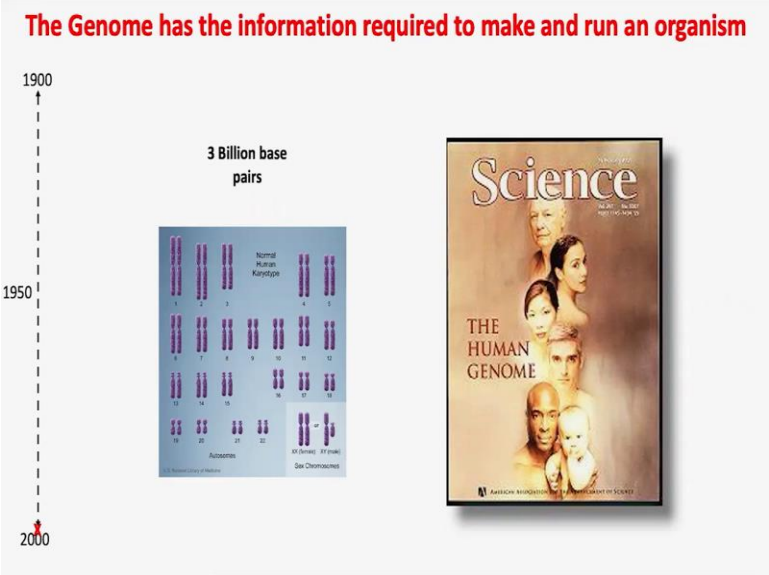

Now, as you are all aware, and this was, this is something you know for many years, and has been touched upon, in the previous part of this course, also, that the genome has all the information required to make an organism and not only make an organism to maintain the organism for a significant period of time. And we know that there are 23 pairs of chromosomes.

And we know that these chromosomes are nothing but pieces of DNA, which I will show you again in the next slide. And these chromosomes look like the karyotype, which you are used to, which is shown over here in front of you, only at the time when they have to be sorted into two different cells at the during mitosis or during meiosis.

And you can see that these chromosomes have characteristic shapes and sizes based on which we have given them some numbers. But the critical part is that we had no clue of what the sequence of these are on, we did not have a complete picture of the sequence of the DNA in these chromosomes, till very recently, about 20 years ago, in the year 2000.

This is the cover of Science the whole human genome was sequenced. And since that time, we at least have the raw data for interpreting what life is especially what why are we humans? Why are we different, but it is quite amazing that at the time, leading up to this sequencing of the human genome, it was believed that sequencing the human genome would tell us everything we need to understand about life. But that has not been so. It is still been a struggle to understand animal development and animal behavior, and basically what makes animals and plants the way they are.

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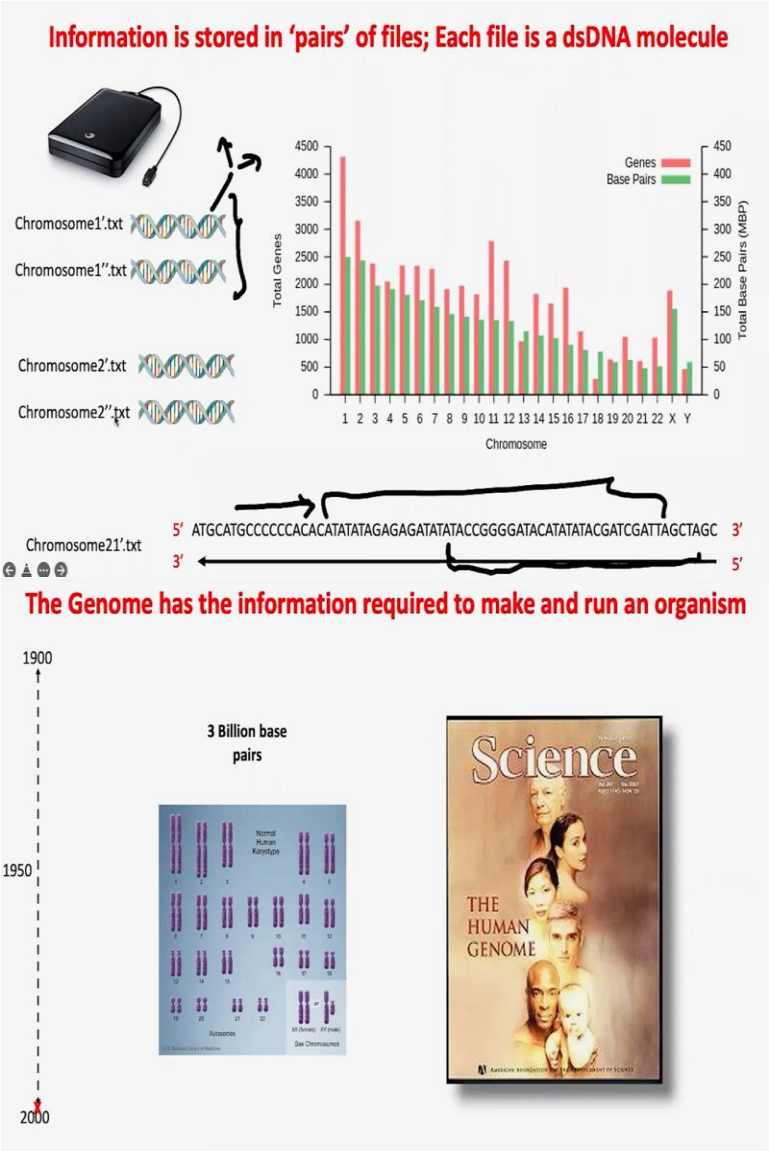

So, to give you an analogy, again, this is very important to get a understanding of what we are looking at, I have already told you that information is stored in DNA in simple using the code of four base pairs. Now I want to take an analogy of a hard drive external hard drive hard drive in your phone or in your computer.

And what I am going to state is that if you imagine that there are two text files, we will call them chromosome one prime and chromosome one double prime, which are basically 95 percent identical, they are very much identical. They are very, very minor differences between these two files. And these two files contain sequences from which are polarized from 5 prime to 3 prime, this is the way we write them.

And there is of course, opposite complementary sequence. And do remember that even though this is information, it is kind of redundant. The utility of this information for genetics is not, what I mean by that is that you will have a gene, for example, at some location in the genome, and do remember that you can have a completely different gene on the opposite strand of the genome.

So, you can have genes transcription from one strand, and you can have transcription from another strand. So, you have two strands, with one strand defining the other strand. And we call this chromosome 1 prime dot text, for example, and there would be a second file. And let us say both these files are kept in a single folder.

And what each of these files represent and this is what I am coming to is basically they represent a chromosome. And each one of them is what we call as a homologous chromosome. In heredity chromosome 1, One of them comes from in humans, for example, comes from your mother, other comes from your father.

And both of them are pretty much the same, but they are not identical. When this chromosome divides into two, and I will come to this again in the next slide, then definitely the two copies are 99.999999 percent the same because it is a faithful replicate apart from errors, and we give the terminology sister chromatids to this and the terminology to these two is basically homologous chromosomes.

So, similarly, you can imagine that all the information which makes us is in 23 files, pairs of files, labeled chromosomes, 1, 2, all the way to 23. And genes are coded on these chromosomes.

Now, here is a graph, which gives you an idea of the number of genes on each chromosome. On the left hand side, the y axis shows you that.

For example, there are 4300 genes on the first chromosome, and barely about 200 genes on the 18th chromosome, so it is not very rich, in terms of the number of genes, this also tells you the total base pairs, mega base pairs in each of these chromosomes, you can see that in green X chromosome is pretty large, first chromosome is pretty large, so is the X chromosome, the Y chromosome is pretty small. And I guess the smallest chromosome is chromosome 21.

So, this gives you a broad idea of the number of genes on each chromosome, the size of each chromosome. And of course, we have approximately 3 to 3.2 billion base pairs in total in our genome. And what I am going to be talking to you about is to try and put Mendelian genetics in the context of chromosomes and genes.

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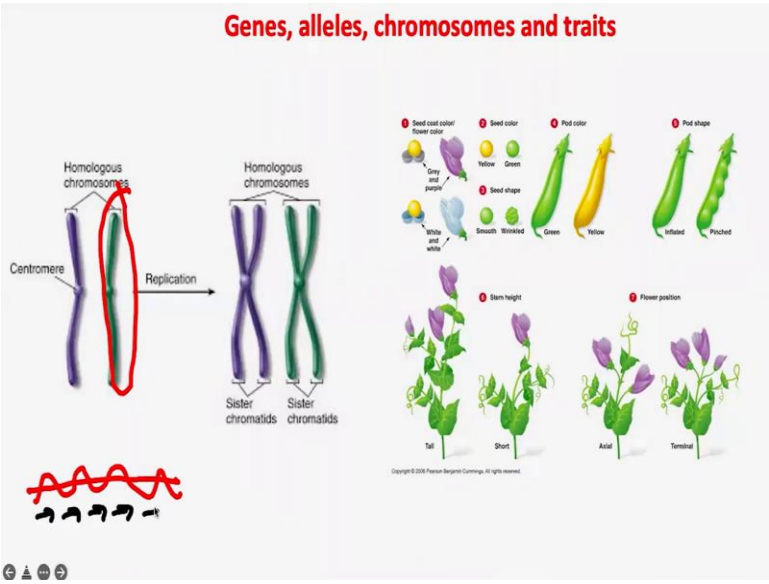

Now, each one of these chromosomes, which I talked about, is basically called as a homologous chromosome. And there is this feature, which consists of repetitive DNA called the centromere, which is, at some point along the chromosome in most chromosomes, and these two are homologous chromosomes, they are nearly identical, but not completely so.

And during replication each homologous chromosomes is built to divide and give you a pair of sister chromatids. And when division takes place, one of the purple and one of the green will go to one cell and another of the purple and another green will go to another cell.

And very obviously, even though you are used to seeing physical features, this is a condensed chromosome. Pretty much each chromosome over here is nothing but is a single strand of double stranded DNA. And in the single strand of, double strand DNA, if I may draw it like this. You basically have genes which are on this DNA, and they can go in both directions. So, if this is clear, let us now move on to what Mendel did?

So, what Mandel did in his backyard was to cross peas to one another, and he looked at certain characteristics. Remember, pea plant was not the only experiment he was doing. In general Mendel did a vast range of experiments working on many different plants and animals.

And the peas plant gave him a set of results. Which were simple, easily explainable and reproducible, which is why we tend to hear a lot about his experiments with pea and not his experiments with other crosses, which were much more confusing, and not as easily understandable as the classical well known pea plant crosses.

So, he looked at pod color, I do not have to define what a pea is for you. He looked at pod shape, he looked at seed color, he looked at seed shape. The famous tall versus short pea plant, and flower position, axial terminal, and so on and so forth. So, these were the phenotypic characteristics which Mendel basically followed in his crosses.

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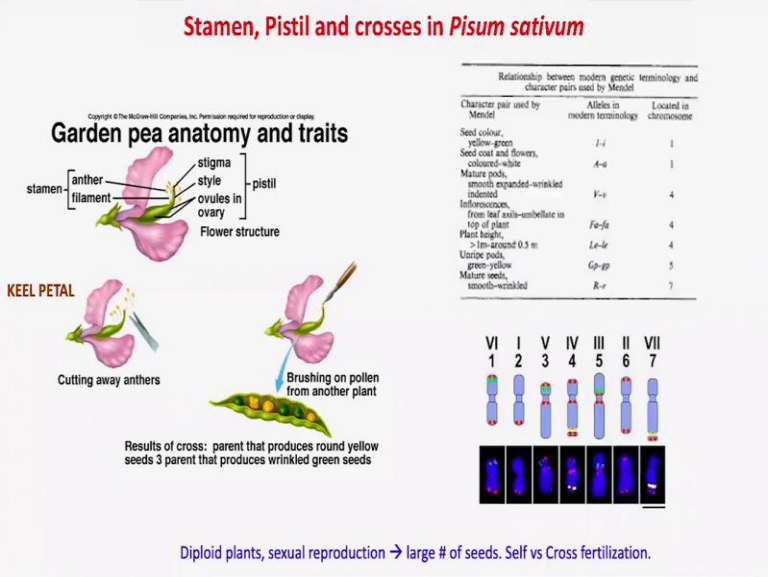

Part of the problem was that the pea plant basically, is a hermaphrodite in the sense that both the male and the female gametes are made in the same flower in the same keel petal, and self reproduction. Clonal reproduction, basically, from the same plant, sperm and egg will fuse and give the next generation is very normal.

So, in order to define and regulate his crosses, Mendel had to do a lot of work, you would have to go to his plants, while they were still maturing, he would remove all the anther filaments so that they were no sperms produced over here. And then he would take anthers from another plant, when he was setting up across and brush the pollen from that plant to this plant, thus regulating the kind of crosses he would be doing.

These are again, the list of characteristics he followed. And as you know, peas have 7 chromosomes and these were distributed, is we know today that these were these phenotypes because of genes which were distributed on different chromosomes. These are this is just a picture showing you the 7 chromosomes, which are there in the pea plot. So, he could do self fertilization, he could experimentally remove anthers and do cross fertilization. And this is the basic way by which he did many of his experiments.

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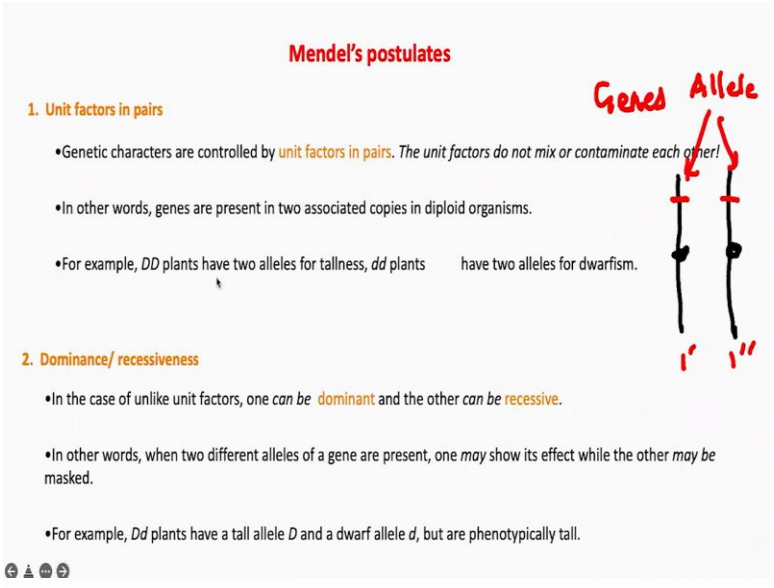

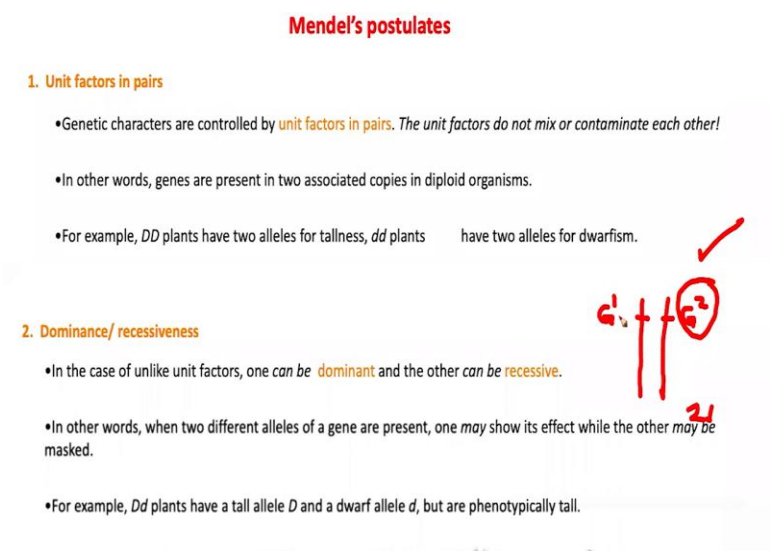

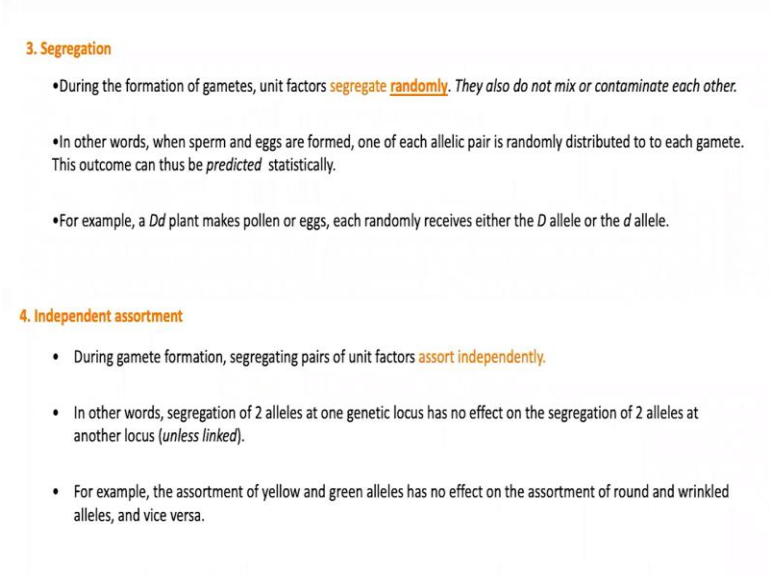

So, what are Mendel's postulates? Now I am going to state them and also try to state the modern view of this. And if any of you has any doubt, I would recommend that you start asking me questions. So, Mendel said that the unit factors which he was tracking, which was basically he was tracking what we know today as genes, but no way of seeing the genes.

Remember, this is 1865, we are pretty much nearly 90-95 because of away from the structure of DNA, we are also almost 90 years away from the belief that DNA has anything to do with heredity even that was not clear till the 1950s. So, he was basically working agents blindly, which were inside the pea plant, he had no idea what these units of heredity were.

But he could see the result of these units of heredity and changes in these units of heredity in the phenotype in the visual things which he saw in the plants. So, genetic characteristics are can controlled by unit factors in pairs, the unit factors do not mix or contaminate each other. This was very interesting, because earlier for many years, it was believed that when you cross.

Let us say, a large cow with a small cow, small cow gives you more milk and you want a large cow or a medium sized cow, which gives you more milk you what the belief was that there would be mixing of characters, whereas Mendelian ideas, told us that whatever we are looking at were contour units of heredity. So, the view right now is that we are looking at two homologous chromosomes, and rather more here, which is what all of us have in our body, which more diploid animals have, and whatever characteristics we were following was of a gene.

So, he worked with one gene at a time, and this gene would be in some location in the chromosome. And the genes could be identical, absolutely identical. Or they could be slightly different. And if they were slightly different, let us call this chromosome 1 prime. And let us call this 1 double prime, then this, if there was a little difference in this gene, let us say three bases were different.

And these three bases caused a different caused the protein made by the gene product to be slightly different, then we would say that this was an allele pair. So, basically, this was a single gene with two alleles and these two alleles were not identical to each other. So, this is the kind of logic which he came up with.

So, now, the second thing Mendel postulated, and is the idea that if you have two alleles, one can be dominant, and the other can be recessive. And if you in a pair of, if you have these two chromosomes, let us take chromosome 21 again, and for the same gene, you have allele 1, so we will call it gene allele 1. And here it is gene allele 2.

And it is what Mendel saw that one of these alleles, if it is present with another allele, this allele defines what the plant is going to look like. Or this allele defines whether again, skin color is a bad idea whether I am going to be dark brown, or light brown. So, one allele, seems to dominate over the other allele.

And the third thing, which Mendel talked about, was segregation. So, now for sexual organisms, gametes usually contain only one set of chromosomes. So, they will not have both of the homologous chromosomes, they will have only one of the copies of the two copies, which are currently present in our genes.

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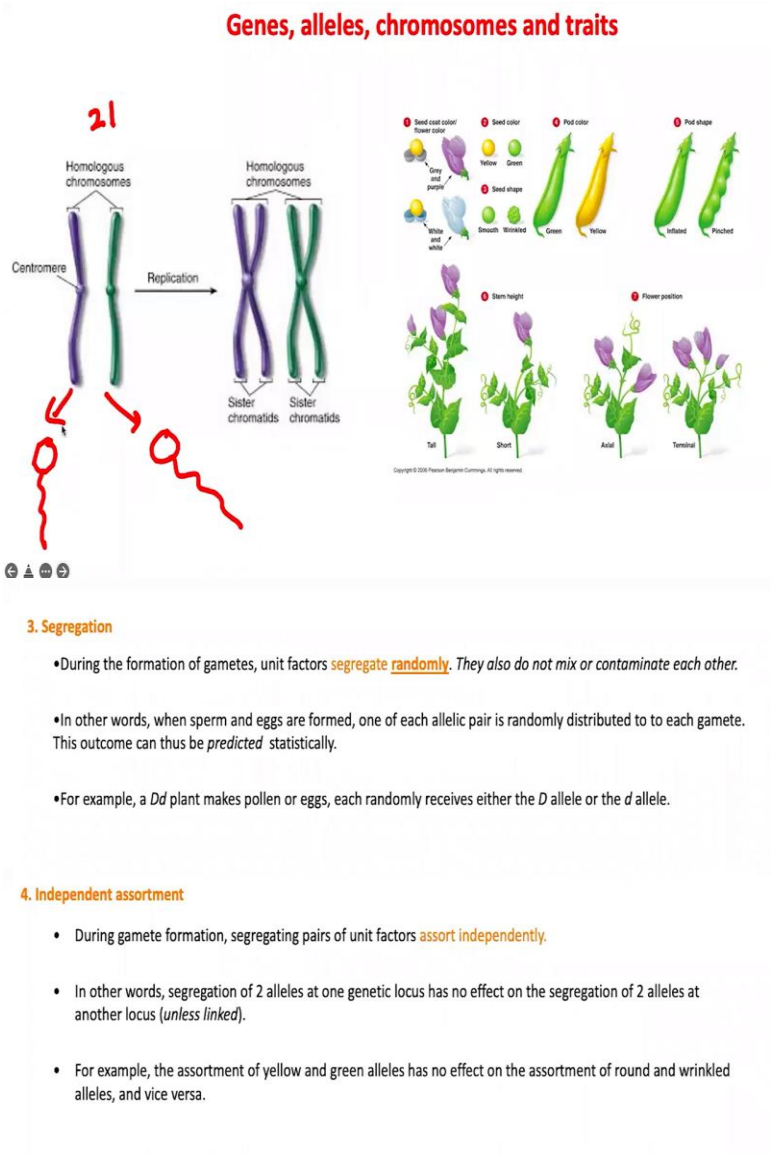

And these, when sperms are made this chromosome goes to one sperm, and this chromosome goes to another sperm. So, effectively, a sperm will have only either purple or green, let us call this chromosome 21 again. So, it will have only one copy. So, if there are any minor changes between these two homologous chromosomes, these are not effectively the minor changes remain in the sperms. And in the next generation, these minor changes tend to continue. So, that is the law of segregation.

And the fourth one is that these pairs of unit factors. So, instead of talking about unit factors, which is nothing but allele, these pairs of unit factors, which is basically a gene will assault independently.

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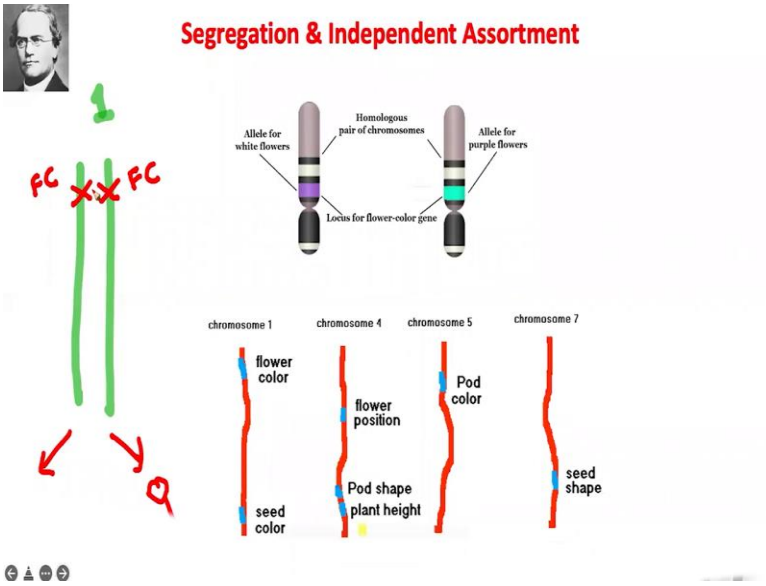

So, now, here are four of the chromosomes in the pea that the genes now one gene coded for one phenotype. So, for example, flower color, there was a single gene seed color, there was a single gene flower position, there was a single gene, pod shape, pod color seed shape, all where the relationship between what he saw and the gene which was deciphering that phenotype was basically a single relationship, which is not true for most of the genetics, which is done, for example, in our body.

This was one of the reasons why Mendelian genetics on the pea plant was fairly straightforward. But for the purposes of this discussion, we now know that his genes were on chromosome 1, 4, 5, and 7.

Now, if you look at pod color, and you look at flower position, these are two different genes on two different chromosomes. So, the law of independent assortment, basically says that pod color and flower position do not influence each other. This is not true for all genes in modern genetics, many times one trait in our body.

For example, I am just making random examples, whether our hair is black or not, and how long our fingers are maybe related, because the genes which are regulating both these features may be the same. And I will explain why they may be the same.

But in all the Mendelian experiments which he did, or at least the Mendelian experiments, the parts he presented because there were simple to interpret. In his paper, the genes for pod color flower position for a flower color are all independent of each other. Because they were on different chromosomes which is why we say that the pairs of traits or the genes did not influence each other's phenotype, they assorted independently.

Now what is segregation? Segregation now refers not to the genes but to the alleles. And what segregation means is that if you have a pair of homologous chromosomes, let us take chromosome one over here as an example, and let us take flower color here as an example, and you have a gene for flower color over here, if these were two independent alleles.

So, let us call this FC gene flower color gene. Let us call this as FC gene, if these were different in their sequences, and one of them was malfunctioning, let us say, basically, what he said is that these two chromosomes segregated independently in the sperms. So, one allele will go to one sperm and another allele will go to another sperm.

And one could tell it was statistical which of these sperms would fuse with an egg to make the next generation because both these sperms would not fuse only one sperm would fuse to one egg. So, the Law of Segregation basically talks about the fact that there are a pair of homologous chromosomes alleles, which are basically copies of the same gene the move physically apart from each other when they go to the sperms or the eggs. That is the law of segregation.

The Law of Independent Assortment says that the phenotypes which were related to individual genes move independently of each other, and the reason is they are completely on different sets of chromosomes.