Cell Biology: Cellular Organization, Division and Processes

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Lecture 19

Meiosis Part I

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Hello everyone, this is Kshitiza from Department of Biochemistry, Indian Institute of Science. I will be talking to you about an extremely important and very interesting form of cell division called meiosis. You would recall from your school biology textbooks that cell division is a critical process in growth, development, repair and reproduction. You have been taught at great length about another form of cell division, called mitosis, in Professor Shikha's previous lectures.

So, I would start by asking you why do you think an entirely different form of cell division called meiosis occurs, when mitosis is already there? Now imagine, when you were a zygote, you received half the number of chromosomes from the egg cell, which came from your mother and half the number of chromosomes from the sperm cell, which came from your father. Now hypothetically, if the egg cell had diploid number of chromosomes that is 2n and the sperm cell also contained diploid number of chromosomes that is 2n, the fusion of the egg cell and the sperm cell would form a tetraploid zygote, which would be the abnormal number of chromosomes and is not found in human baby. Therefore, an entirely different form of cell division called meiosis evolved, which made sure that the number of chromosomes in the egg cell and the number of chromosome in the sperm cell is half the number of chromosomes present in the zygote, which is diploid that is 2n such that the ploidy is maintained in the offspring.

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Now as you can see, here the difference between mitosis and meiosis occurs in three important aspects. Starting from a diploid cell which has a ploidy of 2n in both the cases, DNA duplication is a common step, and after DNA replication the number of chromosomes stays the same in both mitosis

and meiosis. However, the content of the DNA is now doubled. I have shown here 4 chromosomes per cell; four chromosomes shown in different colours.

And the DNA is duplicated, you see that the chromosomes are shown in form of two chromatids which are called sister chromatids, which are joined together at a point called centromere. When mitosis and meiosis are compared, after DNA replication in the mitosis process there is only one round of chromosome segregation. However, in meiosis one round of DNA replication is followed by two rounds of chromosome segregation, which results in formation of four daughter cells as you see here with a ploidy which has half the number of chromosomes as compared to the parent cell which had 2n number of chromosomes. This is in contrast to mitosis where only two daughter cells are formed which have a ploidy, which is exactly the same as the parent cell.

The second very important aspect is, during the meiosis process the two homologous chromosomes that is the version of chromosome one received from the mother and one received from the father pair together, and during the first meiotic division, which is called meiosis one these homologous chromosomes segregate and during the second meiosis division which is called meiosis 2, the sister chromatids segregate. I have shown here two pairs of homologous chromosomes in purple and in green is one pair of homologous chromosomes in black and in pink is another pair of homologous chromosomes.

After meiosis 1, one of the daughter cells contains one pair of homologous chromosomes, which has been segregated and another daughter cell contains another pair of homologous chromosome, which has been segregated and this is called a reductional division. Meiosis 2 is almost similar to mitosis in a way, that the ploidy does not change, from these two daughter cells to the four daughter cells that are formed here.

The third very important aspect of meiosis, which is different from mitosis is, when the homologous chromosomes pair, there is an exchange of genetic material between the two homologous chromosomes. This process is called crossing over and it occurs via a DNA recombination process.

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Let us dive deeper into the different stages of meiosis. Just like in mitosis there are different stages of the meiotic process. Starting from a diploid cell in the G1 phase, as you see here, in S phase the DNA is duplicated, which is followed by a G2 phase where the homologous chromosomes start to align with each other. After G2 phase, meiosis 1, which is also called a reductional division starts prophase 1 of this meiosis is different from mitosis in a way that in meiosis the prophase one is quite long because the homologous chromosomes need to pair together and DNA recombination has to occur. In prophase one the homologous chromosomes pair and crossing over happens. It is followed by metaphase one where the paired homologous chromosomes align at the equator, which is followed by anaphase one where the homologous chromosomes segregate and each of the homolog is segregated to different poles, opposite poles.

Anaphase 1 is followed by telophase 1 and cytokinesis 1 where the cytoplasm divides. Now note, that since the green chromosome and the purple chromosomes are homologues of each other, they will never be segregated towards the same pole. Similarly for the black chromosome and the pink chromosome, they will not be segregated towards the same pole. However, it is entirely possible that the green chromosome here is segregated with a pink chromosome here, which will lead to the purple chromosome here segregating with the black chromosome here. Therefore, this is one of the combinations that I have shown here, the other combination is equally possible. This is one level where merely on the basis of chromosome segregation different types of gametes can be formed and genetic variation is maintained. Now since I have shown here only two pairs of homologs.

You should remember that in human cells there are 23 pairs of homologous chromosomes, which would lead to an enormous number of possible combinations and therefore an enormous amount of genetic diversity merely on the basis of chromosome segregation.

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Now meiosis 1 is followed by meiosis 2. Meiosis 2 is also called equational division because it is very similar to mitosis. Now that the chromosome number in the daughter cells has already been halved during meiosis 1, during meiosis 2 four daughter cells are formed from these two daughter cells and the chromosome number now stays the same. During prophase 2 of meiosis 2, new spindle forms around chromosomes as you see here and in metaphase 2 these chromosomes align at the equator. As we saw in anaphase 1 of meiosis 1 homologous chromosomes segregate towards opposite poles. During meiosis 2 and anaphase 2 in meiosis 2, sister chromatids segregate towards opposite poles. So, the connection between the sister chromatids that was characterized by the presence of centromere here, this connection is lost, and the sister chromatids are pulled towards opposite poles, as you can see here.

Now as we saw in meiosis one there were different combinations possible for the segregation of homologous chromosomes, and that led to formation of different types of gametes. Similarly in meiosis 2 when the telophase and cytokinesis 2 occur, the cytoplasm divides and 4 haploid cells are formed. Different combinations of segregation is possible and this will lead to different combinations formed in these haploid cells. This is another level of genetic variation and this is one very important reason why meiosis evolved in the first place.

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The meiotic prophase is a beautiful process in itself, and it is so intricate that it has been subdivided into five different stages as you see here. The first stage is the leptotene stage. Now after the DNA has been duplicated in the S phase, the DNA still exists in form of thread like structures called chromatin. During leptotene stage the chromatin condensation occurs and now chromosomes are formed.

I have shown here one pair of homologous chromosomes where the first is purple in colour and the second is green in colour; as you see here chromatids from one of these homologues are called sister

chromatids, while chromatids from two different homologues in the pair are called non-sister chromatids. The leptotene stage is followed by zygotene stage. In the zygotene stage the nuclear membrane starts disintegrating; also note that the homologous chromosomes have started to align with each other. Now this alignment of the homologous chromosomes leads to formation of a structure, which is called a bivalent. The pairing of the homologous chromosomes or the coming together of these homologues is facilitated by formation of a proteinaceous complex, which is called a synaptonemal complex. The synaptonemal complex is proteinaceous in nature and is composed of proteins, which are responsible for not only keeping these homologs together but also regulating the DNA recombination between these homologues.

The zygotene stage where the formation of the synaptonemal complex is still immature, is followed by pachytene stage where the synaptonemal complex formation is matured. These homologs are glued together such that the distance between them is now almost 100 nanometers. This is an ideal situation for DNA recombination; note that DNA recombination should only occur between non-sister chromatids and not between sister chromatids. This process is also highly regulated and it involves many proteins of the synaptonemal complex itself. The points of exchange of genetic material between the homologs is marked by these points of association and these are called chiasma. Now I have shown one homolog pair here and one point of crossing over, one chiasma, however there can be multiple points of crossovers between one pair of homologs.

However, the number of crossovers between one pair of homologs is highly regulated. So, the pachytene stage is marked by the formation of the synaptonemal complex and crossing over between homologs. Pachytene stage is followed by diplotene stage; now after that exchange of genetic material is over between the two homologues, it is essential that the homologs need to be separated from each other and this glue needs to be removed.

In order for this association between the homologs to be removed, there is disassembly of synaptonemal complex. So, the proteins that were initially recruited between these homologues are now de-recruited from these homologues, in order for the homologs to separate during anaphase 1. During diplotene stage, the crossing over is completed and the synaptonemal complex disassembly begins. However, the homologs stay connected only at the points of crossing over, which are the chiasma. The separation is completed during the diakinesis stage where the homologues completely separate from each other and the nuclear membrane is completely disassociated. Note that we started with a parental combination of genetic material here in purple and green and we ended up with a slightly or you know majorly different combination of genetic material in the daughter cell here, and this is an extremely stunning process.

We will see how DNA recombination occurs but before that we would see how the synaptonemal complex formation happens.

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What you see here is a schematic of the synaptonemal complex as observed in budding yeast by scientists during meiosis. We have already discussed that in order for the two homologous chromosomes to stay together, a proteinaceous structure called the synaptonemal complex

assembles between them and keeps them in a close proximity such that the distance between them is almost 100 nanometers.

Now let us see what are the protein components that make up the synaptonemal complex in budding yeast? What you see here are chromatin loops from one homolog in the pair and these are the chromatin loops from another homolog in the pair. The first type of elements are called lateral elements; the lateral elements are majorly composed of two proteins called Hop1 and Red 1.

By research, it has been shown that Hop1 protein can actively bring together two different DNA molecules and keep them in close proximity while Red 1 is also essential to maintain this glue and both of these proteins are absolutely essential in regulating recombination in such a way that they bias the DNA recombination between inter homolog rather than between inter-sister chromatids.

The second type of element called the central element is composed of two different proteins called Ecm1 and Gmc2 and the final structure is kept together by a third type of filament called transverse filament, which is composed of a protein called Zip1 budding yeast. Now it is very important to note that the entire assembly of the synaptonemal complex is evolutionarily conserved. By that I mean that the proteins that are involved in the formation of the synaptonemal complex have homologues from yeast to mammals.

So, a synaptonemal complex is not only evolutionary conserved structure it is also functionally conserved. We have also seen that during anaphase one, after the DNA recombination is complete the homologs need to segregate from each other. Therefore, the timely loading of these proteins to the chromosome axis is essential for assembly of the synaptonemal complex and the timely removal of these proteins from the chromosome axis is absolutely essential for the disintegration of the synaptonemal complex in order for the homologs to separate during anaphase one.

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Now that we understand the structure of the synaptonemal complex, let us look at the dynamics of the synaptonemal complex in budding yeast in context with the different stages of meiotic prophase 1. What is shown here in white are two sister chromatids from one homolog in the pair, and what is shown here in blue are two sister chromatids from another homologue in the pair.

Chromatids from two different homologues in the pair are called non-sister chromatids, and recombination is biased towards recombination between inter-homolog rather than inter-sister. During the zygotene stage we know that the synaptonemal complex assembly starts by loading up the proteins that we just saw. During pachytene stage, the synaptonemal complex assembly is matured and the two homologues are brought close together and crossing over occurs.

Now in order for the homologous chromosomes to segregate during anaphase one synaptonemal complex disassembly is equally essential and this is brought about by removal of the proteins that were involved in maintaining the synaptonemal complex here. The synaptonemal complex disassembly is brought about during diplotene and diakinesis stage. In case, the synaptonemal complex disassembly does not occur properly, it can lead to a situation where one of the daughter

cells would get an abnormal number of chromosomes or one of the daughter cells would not get any chromosome at all and such situations are called situations of non-disjunction.

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Approximately 10 to 30% of fertilized human eggs contain an abnormal set of chromosomes, and this is a result of non-disjunction of chromosomes during meiosis. Non-disjunction or mis-segregation of chromosomes can occur either during meiosis 1 or during meiosis 2. You would recall that during meiosis one homologs are the ones that segregate. While in meiosis 2 sister chromatids are the ones that segregate to the opposite poles.

Now in a normal scenario in the meiosis one the two homologs segregate two opposite poles and the two sister chromatids segregate to opposite poles in meiosis 2 normal situation. When non-disjunction or mis-segregation occurs, what happens is, for example in case of true non-disjunction the two homologues, which are paired together are segregated towards the same pole, which leads to aneuploidy.

Similarly, in achiasmate non-disjunction, which happens during meiosis 1, the homologues which are not actually paired together, segregate towards the same pole which again leads to aneuploidy. There can also be a case of premature separation of chromatids during meiosis 1, which could lead to polyploidy in one daughter cell and aneuploidy in one cell. Both of these cases of aneuploidy and polyploidy are deleterious to the organism.

In case of meiosis 2 if non-disjunction occurs, which means that the two sister chromatids did not separate from each other as should be, and both of them are segregated towards the same pole leading to aneuploidy. Aneuploidy and polyploidy result in either miscarriages or result in genetic disorders.

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Coming back to the primary question, which is, if the siblings have the same parents why are they different from each other and how does this exchange of genetic material occur between the chromosomes? The answer to both of these questions lie in a process called homologous recombination and we will be elaborating on the mechanistic process of homologous recombination in the next segment.