Biology for Engineers and other Non-Biologists
Professor Madhulika Dixit
Department of Biotechnology
Indian Institute of Technology, Madras
Lecture Number 12
Cell Cycle

So hello again and in today's class we are going to talk about the process of cell cycle. Now before I get into what is cell cycle and what are the different features of cell cycle, let's start looking at how we start our lives. Now we all know that we start our life as a single celled organism that is the zygote and this happens after the fertilization of sperm with ova.

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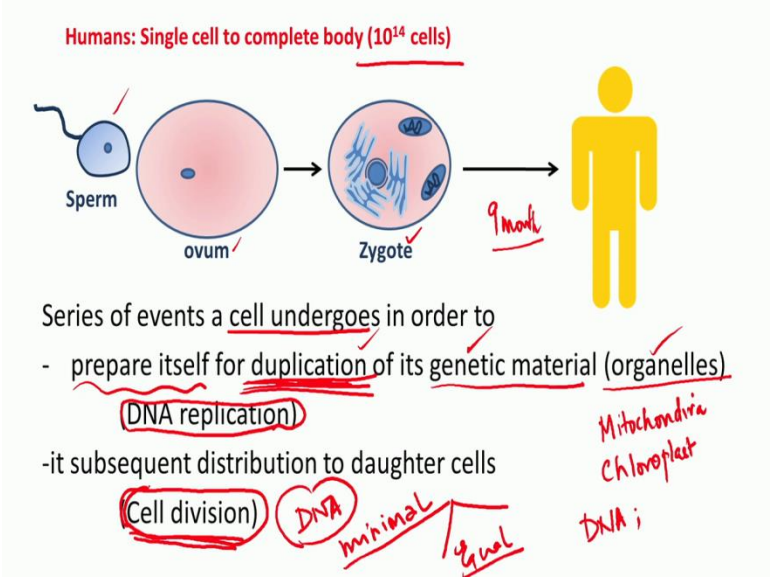

What's interesting is to note that though we all start our life's journey as a single cell in our mother's womb, in about nine months' time, we are born, and then later as we grow and become an adult, our body is made up of roughly ten to power fourteen cells. Now how is that possible?

Now this is possible because every living cell has one basic function to do, and that is to replicate its DNA and then pass it on to the daughter cells. So cell cycle basically talks about how a cell prepares itself to duplicate its DNA and then, to divide into two daughter cells. So, this is something very interesting. Now, how will you define cell cycle? I would say it's a series of events that a cell undergoes, and it (prep), the reason it undergoes all these events it's because it tries to prepare itself, and tries to generate enough raw materials in the cell for duplication.

Now this is important. For the cell to pass on the information, the duplication of the genetic material is very critical point. So it first duplicates its genetic material, it also tries to have sufficient copies of its various cell organelles. For example, the cell has mitochondria, the cell; in case of plants will have a chloroplast.

So, if a cell has to divide into two daughter cells, it has to pass on the same amount of genetic material, which is DNA. Also, it has to divide all the other cell organelles, so that the new daughter cell which is formed, can do all its functions. So the first thing that a cell cycle involves is the preparation for duplication of the genetic material and this involves DNA replication, we will cover this section of DNA replication in a separate class. Today we'll only focus on the various steps of cell cycle.

So it has to duplicate it's genetic material, it also has to duplicate and give more copies of different cell organelles, and the second stage of cell cycle is the actual process of cell division. So once the DNA has been duplicated, how is it that the same amount of DNA with minimal errors. Now this is important to know that every round of cell cycle, the DNA gets duplicated with minimal errors, and this DNA then gets equally divided into the daughter cells.

Now this division is what you call as the cell division. So cell cycle consists of multiple steps and before I get into the different steps of cell cycle, I just want you to ponder over a few things. Now, it's not necessary that each and every cell of your body will undergo cell cycle at the same rate. And there are in fact, few exceptions where certain set of cells, after they have been formed and they have acquired high level of efficiency, they do not divide, and some of them are the nerve cells.

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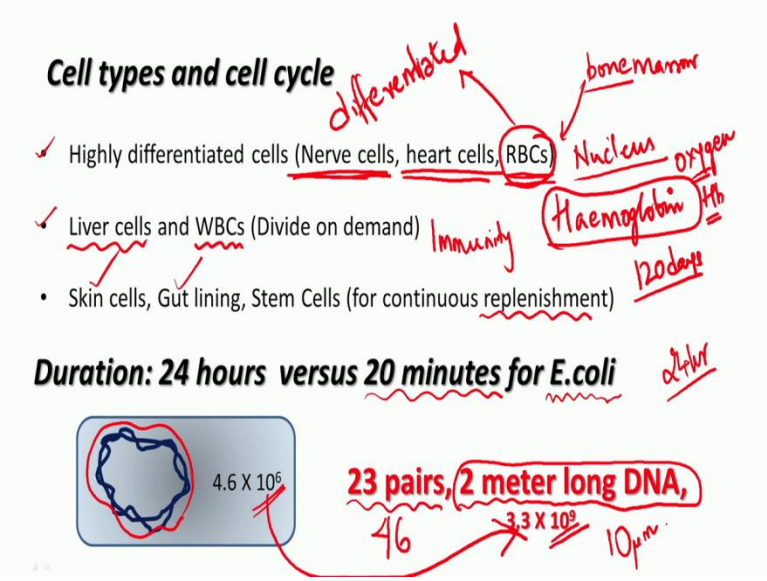

The neurons, once they have been completely formed, except for the few early years of our development, and once they have been totally formed and they have become highly efficient in their function, they do not divide. They, in fact do not undergo the process of cell cycle. I'll come to it as to why, and the reason in fact I would say that they don't divide is because they are too busy doing their function and they are highly specialized, in biological terms we call it as, they are already 'differentiated'.

Similarly, if you look at the cells which form the walls of our heart, the cardiomyocytes, they do not divide after they have differentiated. The red blood cells, these cells periodically come out of the bone marrow, they are formed from bone marrow cells and you find, you must have studied in your school textbooks that this is one cell type which once it has differentiated, once it has reached its (differentia) ability, it loses its nucleus, and that makes sense because the primary function of the (riv) red blood cells is to carry haemoglobin. Now haemoglobin is the main pigment which absorbs and carries oxygen in our blood, and that's its major sole purpose. So if it wants to accommodate more and more amount of haemoglobin, it has to get rid of the nucleus.

So upon differentiation, the RBCs do not have nucleus, and as a result they do not undergo cell division once they have differentiated, and because they do not undergo cell division, each RBC which periodically keeps coming out of our bone marrow pool has a life span of about one twenty days. So, there are certain cells which will not undergo cell cycle. But then, there are

certain cells which undergo cell cycle or cell division only if there's a demand. And one good example is the white blood cells. Now we all know, that every time we get some sort of an infection, our body has an ability to fight it out, which is what you call as 'immunity'. Right?

Now this immunity is possible because every time the white blood cells are sensing the invaders, there is a whole series of events which are taking place in white blood cells, and it allows and triggers now the white blood cells and sends a message to the individual white blood cells that we need to multiply, we need to divide, have enough soldiers ready so that they now kill the invading (my) pathogen or the invading bacteria. So, there are cells in our body which will undergo cell cycle, if the need arises. Same (example), similarly you find that the liver cells, they regenerate, they divide only when the need is.

In contrast to these highly specialized cells, I won't say the other group of cells are not (step) specialized, but then there function is to maintain the body parts. For example our skin. Now if you have any kind of wounds taking place, the skin has to heal itself and it has to repair itself. Now this kind, these kind of cells, which are usually the epithelial cells, the lining cells, the lining of the skin, the lining of the gut, they have to keep on dividing and replenishing the lost cells. So these are the most frequent cells which undergo the process of cell cycle. So, depending upon what is the sole purpose of a given type of cell, lot of cells may choose not to undergo cell cycle unless pushed to do so; while certain cells have to routinely divide and give rise to daughter cells.

And one point to be noted, is that every time they divide and give rise to the daughter cell, they have to pass on the exact information to the daughter cell. Now that is a lot of job and it requires a lot of precision. Before I go again further, I want to again highlight another important point. Now each eukaryotic cell will have obviously different lengths of cell cycle. But if we were to compare an average cell cycle for an average human cell which is anywhere between sixteen to twenty four hours, you find prokaryotes like E.coli multiply every twenty minutes. Now that's interesting because this should also tell you why once you have a bacterial infection, it just spreads so quickly because every two in twenty minutes, the microbe is actually giving rise to two (daghter) daughter cells.

But, unlike humans, and I'll take the examples of humans for simplicity, you find that the bacterial structure is much more simpler, it just has a single molecule of circular DNA, which is made up of about four million base pairs. Now compare this to humans where would have about twenty-three pairs of chromosomes, in total we have fourty-six chromosomes, and if we were to unwind these chromosomes, or the DNA and put it together end to end in, let's say, a lab, you will find that the actual length of DNA from a single cell in humans is probably two meters long. And not just long, if you look at the number of base pairs it has, it's about thousand fold bigger than the prokaryotes.

So our architecture, the architecture of human DNA, is far more complex, and it's interesting to note that our two meter long piece of DNA fits into a cell which has a diameter of about 10 micrometers. Now how is that possible? Now, this is possible and it's important for you to understand this, for understanding both, cell cycle and mitosis and meiosis, so I will cover it right away, is how are these DNA arranged, and they are arranged into chromosomes is all what we know, but there's an architecture which is very different in case of eukaryotes than in prokaryotes.

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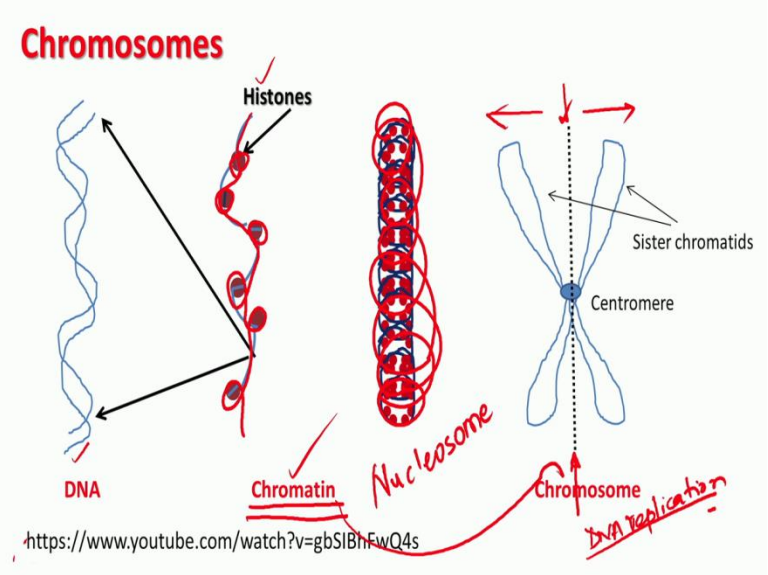

So a DNA which is, in this case, in this light is this molecule. When you want to package it, when the cell wants to package this DNA into a compact structure, this DNA, here it's represented as a string, actually winds around a set of proteins called as the 'Histones'.

So it's like, you have a string of beads, where each bead around that bead, the DNA strand wraps, and those proteins are called as the Histones. Now that's the first order of organization, and then this string of beads will further coil in a helical fashion and pack over each other and they will form nucleosomes, and (nu), so in this case this is one Nucleosome, then it coils again, and the next coiling and so on. Now each of these Nucleosomes get further condensed, and that structure is what you call as the 'chromatin'. So in humans or in eukaryotes, the DNA being more complex, much more bigger in size is packaged through the help of histones, the proteins which help in their packaging and help them in holding in structures called as chromatin.

And each one of us, as I said, have twenty-three pairs of chromosomes, and each chromosome is made up of a (chrome), is has chromatids, and what you find is after the process of DNA replication in cell cycle, we will cover this separately; after the process of DNA replication has taken place, each chromatin will give (ri), sorry, each chromatid will give rise to the sister-chromatid. These are sister-chromatids, but each one of them is actually a chromosome. And, these sister-chromatids, right after DNA replication will be held together at a central point by a structure called as 'centromere'.

Now this is a very important structure, we will refer this to, we'll come back to this when we are talking about cell division and why it becomes very important, because you will find, I have drawn this, let me first rub this a bit. Okay. So if I were to erase out all this, and then again try to highlight to you this axis, right? Now it is here, that the two, at the time of cell division, the chromosomes will separate, and I will come to this when we talk about mitosis. So, you have to appreciate that, unlike prokaryotes, which have much simpler DNA, the DNA architecture is a little more complex in humans, and almost all the eukaryotes and that is because we need to compact all these large amount of information into a tiny cell which has a diameter of about ten microns, and within that, it has to packet into a nucleus which will have a diameter of about two to five microns.

So, that is what, that is how the DNA in our body is organized. Now it is not that throughout the cell cycle, you will find that a DNA always exists as a chromosome. That's not true. Mostly it is organized as a loose set of fragments of chromatin, but right before a cell is ready to divide, and divide it is genetic material, the chromatin gets condensed into chromosomes. So we'll look at all this in our class on cell division. So what is cell cycle? Let's get back to cell cycle.

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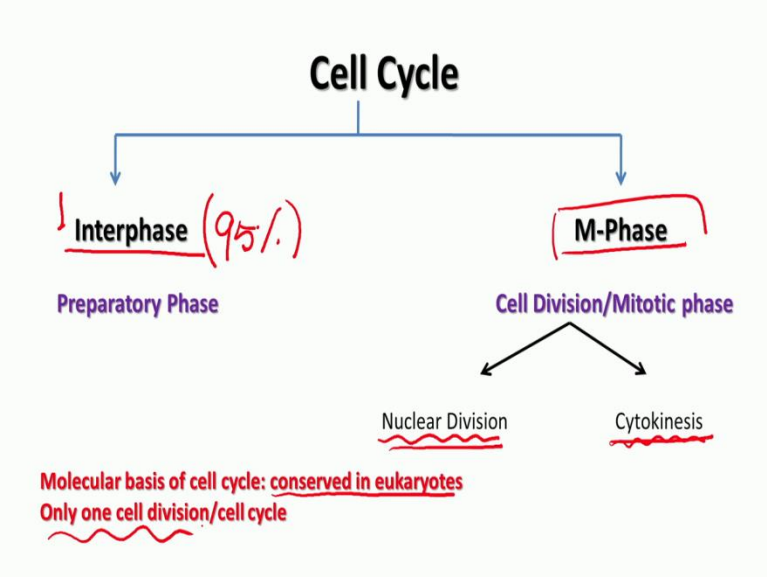

As I told you, the purpose of cell cycle is to ensure that it passes on its exact information, to the two daughter cells, and in the process of doing it, it has to first duplicate it's DNA, and then distribute it to the two daughter cells, it also needs to duplicate it's organelles and distribute it to the daughter cells.

Now, so, this cell cycle consists of two major phases; the first phase is the 'interphase'. Now interphase occupies almost ninety-five percent of the time of a cell cycle, while 'M-phase' is much short lived, and it's in the M-phase that first the genetic material, after being duplicated, the nucleus divides into two nuclei and then the cytoplasm divides and gives rise to two daughter cells. So you have nuclear division, you have cytoplasmic division. Now, one thing which is intriguing and surprising rather, is that if you were to look at the players, the molecular players which govern this interphase, mitotic phase and DNA replication, you find that they are highly conserved in eukaryotes.

So, that's interesting. The second thing is in every cell cycle, the cell undergoes cell division or division of the genetic material only once. So every cell prepares itself, generates enough raw material, gets ready to duplicate its DNA, having generated equal copies of its genetic material it then divides. So, in one cell cycle, the cell division or the nuclear division and the DNA replication happens once. So let us go to the cell cycle. This is a little busy slide, so let me just walk you through this. So let us say, this is the cell which has decided to divide into two

daughter cells and pass on the information to its daughter cells. So, the major part as I told you is the preparatory phase, so all the way from the beginning till here is the interphase. Alright?

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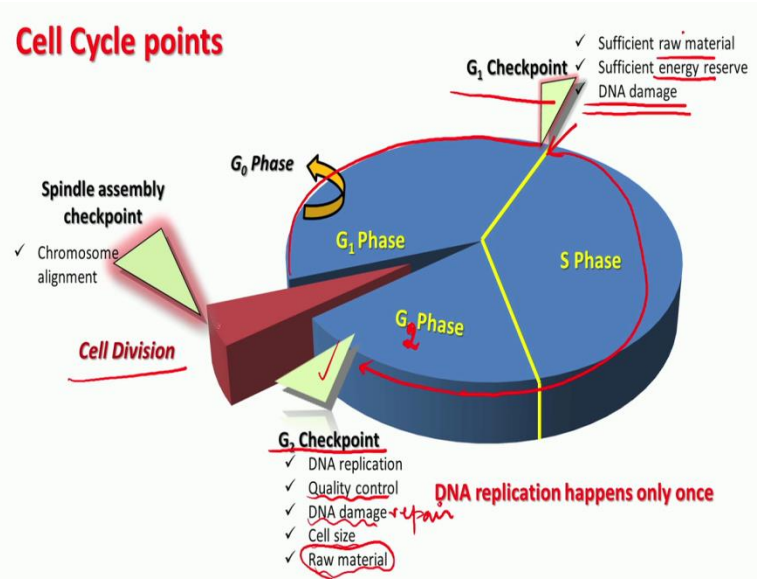

Now in this interphase, we again have three stages, the first one is called as the G1 phase, the G1 phase sorry. The G1 phase. Right? And, it's also called as the growth phase one. Now it is, it lasts anywhere about eight to ten hours and in this phase, the very first phase of the cell cycle, the cell basically starts growing in size, it starts accumulating enough currency, because it will need all that energy to do the subsequent processes, so it starts generating a large amount of ATP, it starts duplicating it's organelles because eventually the organelles have to be passed on the daughter cells, and it generates enough resources.

Now one of the major resources which have to be generated in bulk quantity are the histones, because of the DNA is going to get duplicated, the new DNA has to be organized as a chromatin structure, and for that, lots of histones are required. So the building blocks, a lot of these proteins which are necessary for the process of DNA replication, also for compacting the newly synthesized DNA, for the packaging of the newly synthesized DNA, which is the histones are getting synthesized in the G1 phase. And, before the cell actually comets and starts doing the process of DNA replication, it has to make sure that there is no DNA damage whatsoever. A cell cannot afford to allow a faulty piece of DNA to undergo DNA replication because then, it will

enhance the chances of passing on the non-favourable characters to the daughter cells, which is not accepted, right?

So, in G1 phase, the cell is essentially preparing itself, generating raw materials, generating energy, and, so that now the cell is ready to move on to the phase of DNA replication. So the second phase of cell cycle is the S-phase, where the actual duplication of DNA takes place, each chromosome duplicates itself, and it lasts anywhere between six to eight hours in humans, and we'll cover this topic of DNA replication separately, because it involves a little bit of understanding of how the DNA actually makes sure, that it is passing on the exact information. So I'll cover that in a separate class. But, for the time being, you remember that the second phase of interphase is the S-phase.

Now once the DNA has been religiously and cautiously duplicated, the interphase has the third phase, which is, I am sorry it should be a G2 phase here. The G2 phase. So you have the G1 phase, the S-phase and the G2 phase. Now in the G2 phase, again, remember, the cell has still not divided, it has only duplicated its DNA, and it's ready to divide. But, for it to divide, and it has to, for it to ensure that the chromosomes get properly distributed, right? It needs a whole lot of new machinery, which is the machinery required for mitosis. We'll again cover cell division, there are different types of it, but here in this case it is mitosis.

And for mitosis to happen, it has to make sure that the sufficient raw materials which are required to carry out the process of cell division are getting synthesized. Again, there is sufficient energy available with the cell to commit itself to the next step, and a very important part is that it will make sure at this stage that the process of DNA replication has been foolproof. Right? It has to make sure that there has been no errors incorporated due to the process of DNA replication. So a quality control exercise to make sure that all that newly synthesized DNA is intact, consists of correct information, is packaged correctly happens in the G2 phase.

Once that is all proper, the cell is now ready with its duplicated DNA, its duplicated organelles to be divided into two daughter cells, and that is the M-phase. So this is the M-phase, which will last for about an hour. Now the M-phase again has two steps; the first step is where the nucleus divides into two daughter nuclei, that is called as karyokinesis. 'Karyon' means nucleus, 'kinesis' means generation, so generation of two daughter nuclei happens in the first step, which

is mitosis. Once the chromosomes have been now successfully divided into two daughter nuclei, and there is no error happening there, you then, then the cytoplasm actually divides, and that is called as the 'cytokinesis'.

So what's happens is, after the mitosis or the M-phase, you find that the single cell becomes two exact copies as the daughter cells. So, let me again tell you this. So the cell cycle has the major part which is the interphase. Interphase inturn has the G1 phase, the first preparatory phase, the S-phase, when the actual DNA replication happens, and then the second preparatory step, where it is called as the G2 phase. And in this G2 phase, the cells prepare itself to divide, and then the actual process of cell division, which is called as the M-phase. Now, as I mentioned in the beginning, I said some of these cells do not choose to undergo cell cycle like the neurons.

Now these cells perpetually stay in a state of quiescence, or a resting phase. So they do not even enter the G1 phase, they just exit the cell cycle and they stay in what is called as the G0 phase. This is also called as the phase of cell arrest. Now it doesn't mean that in this phase the cells are not living, the cells are living. They are doing the routine job, they are doing their function, but, they are not committing themselves, they are just so busy that they just don't have time to undergo the process of cell cycle in simple terms. So, this is the G0 phase.

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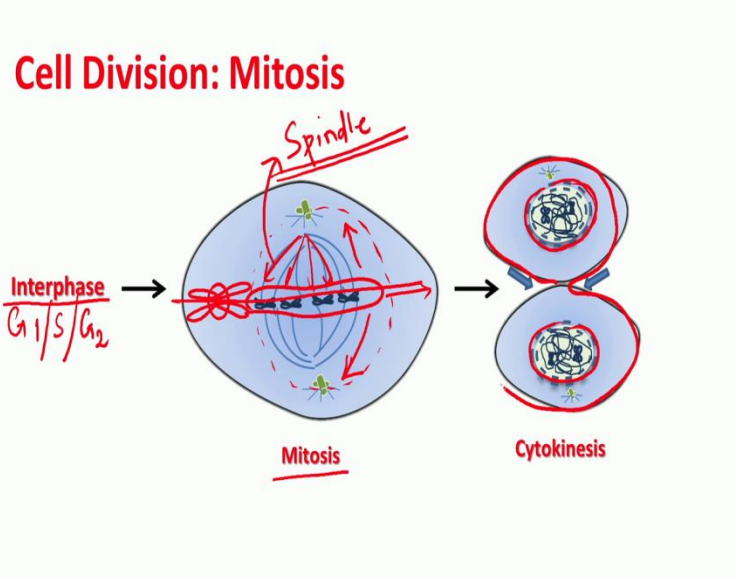

But then, so let me just look, pictorially also depict how the cell division happens. So this is where the interphase happens, there was a G1 phase, the preparatory phase, the S-phase of actual

DNA replication, the second preparatory phase of G2, and then, we had all the chromosomes ready and duplicated. So you can see that each chromosome had given rise to its new copy, and then you had the centromere. Now all these chromosomes, during mitosis or cell division, will align to the equatorial plane of the cell, and you observe here that the nuclear envelope has disappeared. The parent nuclear membrane has disappeared.

And then, there is a special structure formation taking place called as the spindle fibres. Now I'll come to all this when we talk about cell division, but for simplicity in this class, I just want you to understand that after the DNA has duplicated, the chromosomes divide from the equatorial plane towards the two separate poles of the cell, and it is possible because of the spindle structure. These are literally like threads, which are pulling the chromosomes apart. Alright? Like it will like you have these chromosomes arranged like puppets on the equatorial plane, and then there is a tug-of-war, and then the chromosomes get separated.

And then, once they are separated, the nuclear envelope restarts to appear. So you start getting daughter nuclei form, and then, the cytoplasm or the plasma membrane thinches and separates the two daughter cells, which is what you call as the cytokinesis. So, this is what happens in cell cycle, but then, as I said, a cell cannot afford to pass on wrong information, so there has to be very good checkpoints, there has to be some sort of toll gauge, which make sure, that as the cell moves from one phase to the next phase, no wrongdoings have been done. So in cell cycle, there are three major checkpoints; the first check point is right after the G1 phase, alright?

Before the cell commits to enter into S-phase, and in this G1 checkpoint, it will make sure that there is sufficient raw material, there is sufficient energy and most importantly, the cell will make sure that the initial DNA that it's going to duplicate. So the starting material, the starting DNA has no DNA damage. Then the S-phase happens, the DNA gets duplicated, passes on, goes to the G2 phase, right? And, before the cell commits itself to the actual cell division, you have the second check point, which is the G2 check point. Now in this checkpoint, there is a quality control which takes place. This mechanisms make sure that no (mu) unnecessary mutations, or no unnecessary errors have happened while copying of the parent DNA. If at all some damage has happened, then the repair mechanism, the DNA repair mechanism happens.

The cell size is appropriate because now, it has not only divide the nucleus, it has divide the cytoplasm. It has to make sure the organelles are sufficient, that there is a sufficient space and volume available for the parent cell to divide. So that is also taken care of in the G2 checkpoint. And of course, it makes sure that there is a sufficient amount of raw material available for the actual process of cell division. The third checkpoint is actually in the process of mitosis.

I told you, let me go back to the back slide, that the chromosomes arrange at the equatorial plane. Now if these chromosomes, each fourty-six (pair) each fourty-six chromosome manage copy. If it is not properly arranged in the equatorial plane, the distribution is not going to be equal. So, that checkpoint that the chromosomes are appropriately aligned, they are appropriately connected to the spindle machinery, happens at the M-phase and it is called as the spindle assembly checkpoint. So, you find that there are enough checkpoints available in the process of cell cycle.

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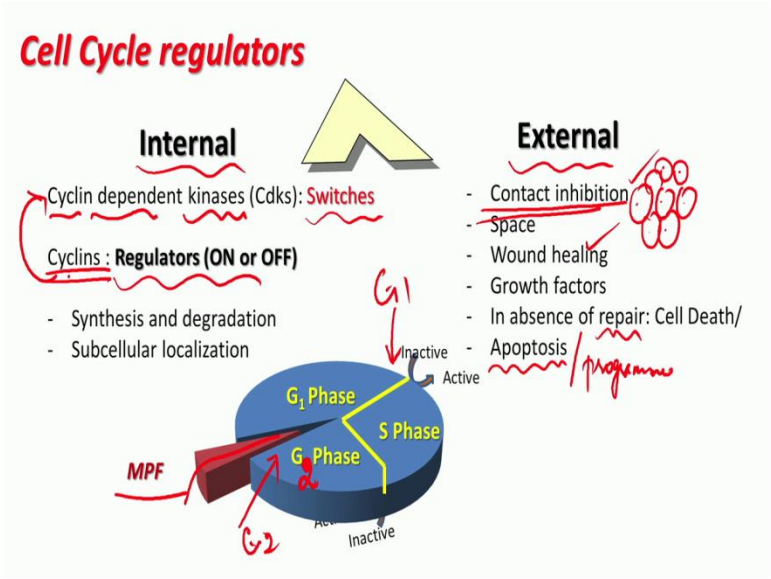

But how are these checkpoints brought about, there are internal and external regulators, to make a more complex information simpler, I just want you to remember that there are enough switches a each of these checkpoints, at the G1 checkpoint, at, I am sorry with the slides, this is a mistake, this is a G2, G2 checkpoint, and at the mitotic checkpoint. There are these switches, which can be turned on or turned off, and these are turned on or turned off by regulators which are called as ‘cyclins’.

So these cyclins, in turn regulate the activity of switches which are called as the ‘cyclin-dependent kinesis’. These are a group of enzymes which keep adding phosphate to proteins, I will not get into details here, but for simplicity, just take it like this, the checkpoints has sufficient regulators in place, and their relative distribution within a cell, their rate of synthesis determines how a cell cycle is regulated.

The external features is, for example if you have a wound created. Now one cell will go on dividing to give multiple cells, but it starts growing as long as the wound is closed. So once the wound has been completely closed, there will not be any further cell division, and this is called as ‘contact inhibition’, which is very often seen in wound healing.

Now, many a times, despite all the checks and balances in place, a situation may happen when a cell is not able to repair the DNA, it's not able to repair the damages done. In such a case, the cell itself takes a call of self-destruction and that is called as ‘apoptosis’, it undergoes cell death, or it is also called as programmed cell death. So it's interesting to see that the cell regulates its own cell cycle, and it also has machinery in place to decide if there are damages happening beyond repair, it's no point passing it on, just self-destruct, and that happens through the process of apoptosis.

So, we saw today that cell cycle is a (ste) is a process by which cell prepares itself to divide and in the process of doing it, it duplicates its DNA first, it duplicates its cell organelles, and then it actually divides to the process of mitosis.

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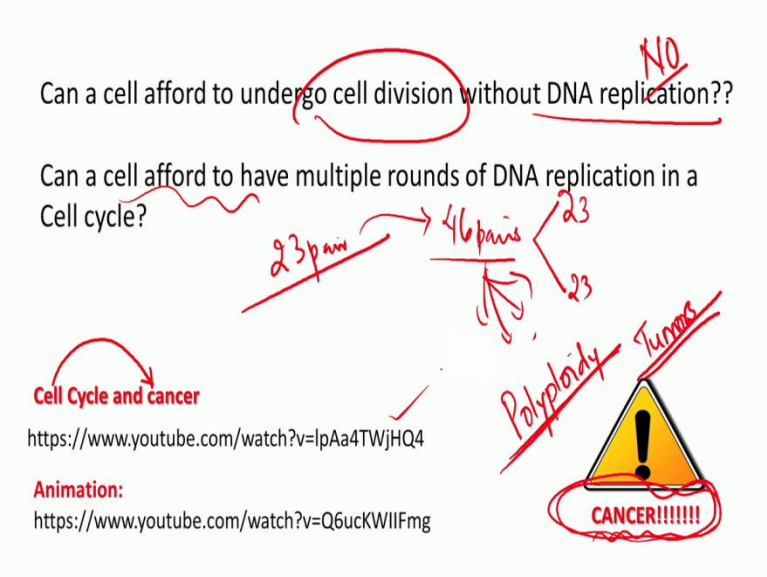

Now one thing I want you to remember is that in every cell cycle, the DNA replication or the DNA duplication happens once, and, I will post this question to you, that can cells afford to undergo a cell division, without undergoing DNA replication. And the answer is 'no, that is not possible'. And it is very obvious because if a cell without even duplicating its DNA is going to divide, it is just going to pass on the chromosomes in a very arbitrary fashion and the two daughter cells will not receive all the necessary information to do the body functions or the organelle function.

So it is not possible for a cell to divide without the process of DNA replication. Similarly, you will find that a cell cannot afford to undergo multiple DNA replications and then divide. Then what will happen? If you are starting with twenty-three pairs of chromosome, right, you are duplicating it, so you end up having fourty-six pairs, right before the cell division, and then each daughter cell again ends up getting twenty-three pairs. But, if it goes on doing these rounds of DNA replications, number goes on increasing, and then when you divide, what will happen is, the daughter cells will not retain the same number of pairs of chromosomes, and that will lead to 'polyploidy'. Right?

Now this is again not good for the body. So naturally, if the cells are not able to regulate their cell cycle properly, we will have a lot of diseases happening in our body and one classic example is 'cancer'. Now these are cells which just lose that control of restraining itself if damages have

happened and destruct themselves. They just lose that ability, they don't listen to the restraining mechanism which asks the cells to die if things are not fine. And as a result, what happens is these defective cells, they keep on accumulating, they become highly aggressive, and you start having a mass of uncontrolled cells, which is what you call as the 'tumors'.

So if you are interested to know exactly how cell cycle is plays a very vital role in progression and initiation of cancer, I invite you to see this video, a very nice animated video in a very simple language. And if you really want to visualize the whole process of cell cycle in an animation, I will recommend you to go through this video. I think with that, we have covered cell cycle, and in our next class, we will actually talk about the process of cell division, that is how exact number of chromosomes get passed on to the daughter cells through mitosis, and then another form of cell division, which is meiosis. So thank you again, and do write back if you have any doubts, you will be given access to our weblink, and we'll see you again next time. Thank you.