Molecular Biology
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Module - 05
Replication
Lecture-24 Mutagenesis and repair mechanism

Hello everyone, this is Dr. Vishal Trivedi from department of biosciences and bioengineering IIT Guwahati and what we were discussing we were discussing about the different aspects of the molecular biology in this particular MOOCs course. So far what we have discussed in this particular module we have discussed about the DNA applications in prokaryotes followed by we have also discussed about the different steps of the DNA applications in the prokaryotic as well as the eukaryotic system. So we have discussed about the semi conservative mode of the DNA applications followed by we have also discussed about the DNA replication machinery in the prokaryotic and as well as the eukaryotic system. And in the last lecture we have also discussed about the importance of the telomerases and the telomerase enzymes and how it is actually helping to fill the gaps within the at the termini of the chromosomes. Now when the DNA replication is happening or even the cell is actually been continuously been exposed to the different types of the mutagenic molecules or the different types of mutations happens within the cell because when the cell is replicating it has a proofread activity it has utilizes that proofread activity to correct the sequences.

But even then there are spontaneous mutations which are going to happen into the DNA and these mutations are actually going to be detected by a well established machinery and that is how it is actually going to participate and it is going to correct those mistakes. You know that if these mistakes mutations are not been corrected they are actually going to lead to the accumulation of mutations and ultimately it may actually cause the development of the different types of the cancers. So DNA damage as the name suggests it could be occurs into a DNA due to the error into the DNA replications it could happen because it caused the spontaneous lesions or it could be because of the transposable DNA or it could be because of the physical mutations or the chemical mutations. Physical mutagens there are several examples of the physical mutagen and there are several samples of mutagen which we are going to discuss and then errors in the DNA replication is also very very important in terms of the DNA damage.

So what is mean by the DNA damage? It is known that the genome is not a static entity right genome is present inside the nucleus or inside the cell right in the case of prokaryotic system and it is whenever you are actually getting exposed to a particular type of physical or chemical environment it is actually getting exposed as well. So and

you know that the importance of the genome right is actually hereditary material so it actually going to follow the information to the next generation and that is not only common so it is important that the genome should be intact and it should not be get damaged. So hence it is highly subjected to a variety of heritable changes. A sudden change in the sequence of an organism genome that give rise to the alternate form of any gene is called as the mutations as a result the DNA get damaged. These mutations are mostly recessive and lethal mutations are random can occur anytime in any of the cell of an organism it is not like that if the mutation occur once the same mutation cannot occur again mutation is recurrent can cause again and again right.

So the question comes how does the DNA damages happens? On the molecular basis DNA can be damaged in two ways some mutation may cause spontaneously some mutations are induced by the mutagens. Spontaneous damage occurs without the treatment of the organism with an exogenous mutagens it is mainly due to an error in replications spontaneous lesions and the transposable elements. Whereas the induced mutations arises when the mutagen react with the parent DNA which causes the structural alternation in base pairing. What is mean by the mutagens? Any agent which causes the frequency of the mutations is called as which increases the frequency of mutation is called as the mutagens. Now as far as the DNA damage is concerned you can have the two main category one is called as spontaneous damage the other one is called as induced mutations.

So within this category you have the multiple components and these components are important for causing the DNA damage. So agents causing the DNA damage you have these agents which are causing the spontaneous mutations and you also have the agent which are causing the induced mutations. Within the spontaneous mutations you can have the errors in the DNA applications you can have the tautomeric shifts and spontaneous lesions within the spontaneous lesion you are going to have the deanimations, depredations and depredimitations and the oxidative cleavage. Whereas the transpositions is another phenomena through which it is actually going to cause the spontaneous mutations. Whereas in the case of induced mutations you are going to have the two different categories which are can cause the induced mutations.

One is called as the chemical mutagens otherwise called as the physical mutagens. Within the chemical mutagens you are going to have the different types of agents which are going to cause the base analogs. So you are going to have the chemical agents which are going to function as a base analogs and that is how they are actually going to destroy the DNA. Then you can also have the deanimating agents you are going to have alkalating agents. Most of the anti-cancer drugs or majority of the anti-cancer drugs are alkalating agents and then you are also going to have the intercalating agents because

they all are actually going to do interfering into the replications and interfering into the repair mechanism and that is how they are actually going to cause the mutations and that mutation will perpetuate from the generation to generation.

Then you are also going to have the physical mutagens. Physical mutagens means the physical parameters what you are going to use. So in that case you are going to have the UV radiations, you are going to have the ionization radiations and you are also going to have heat. So these are the physical mutations which are physical parameters which are actually going to cause the mutations. Now let us first start with the spontaneous mutations and then we will discuss about the induced mutations.

So spontaneous mutations number one category is the error into the DNA applications. So tautomeric shifts. For example so shift of a proton from its nitrogenous base form its rare form and that is called as the tautomeric shifts. The stable keto form of the thymine and adenine and the amino form of the adenine and cytosine undergoes tautomeric shift to form the unstable enols and imines respectively. For example you have the stable form of the adenine and guanine that is the amine form and once it goes from the tautomeric shifts it is actually going to form the immuno forms and these immuno forms are very rare but they are actually going to be less unstable.

These forms are very short lifespans if they are incorporated into nascent DNA they may result into the mutations. And these bases are present in their unstable enol or the immuno state they tend to form the AC and GT base pairing. This AC and GT base pairing is not allowed and that is how it is actually going to destroyed or it is actually just going to distort the DNA structures and because of that for example this is C it is actually going to form the interaction with the A form. So A is always making a base pairing with T in the DNA but in this case A is actually going to make a pair with C and that is actually going to cause the alteration into the sequences and that is how it is actually going to go into the next generation. So imagine that you have a C so instead of if you have a C into the template ideally it should be G into the replicated DNA.

But since this kind of mutation is happening or this kind of tautomeric shift is happening what will happen is that C is actually going to give rise to a synthesis of A. So instead of A instead of G you are going to have A into the DNA sequences and that is how it is actually going to cause the mutations. The net effect of such event and the subsequent replication required to segregate and mismatch pair that is the AT to GC or GC to AT base pairing substitutions and that is how it is actually going to cause the mutations. Mutations via the tautomeric shift in the basis of DNA in the examples a guanine undergoes a tautomeric shift to a rare in all form at the time of replications. In its in all form it is paired with the thymine.

So this is what exactly is what is showing here that you are actually replicating a sequence where you have the all sort of nucleotides like G, C, T and all that and during the replication if the G is actually getting converted or tautomeric getting shift into a in all form then G is actually going to start making a pair with T instead of G is going to start making pair C. And because it has altered the base pairing information it is actually going to allow the formation of the instead of GC it is actually going to give you the AT because it is actually going to give you the T instead of G and as a result it is going to propagate. So once the DNA replication is going to happen of this particular sequence it is actually going to give you the in the wild type it should be G is actually going to give you the C but in this particular type of second generation instead of G and C it is actually going to AT. So this is what exactly happened when you are going to have the tautomeric shifts. So during the next generation the joining shift back to its more stable keto form thymine incorporated opposite the in all form of the guanine direct the incorporation of the adine during the subsequent replication.

The net result is that GC is going to be AT mutations. So G is making a base pairing with T so as a result in the first generation the T is going to be synthesized and then in the second generation G is again reverting back to the in all form into the into the keto form. So because of that it is actually going to start again synthesizing the G to C but here instead of T it is actually going to since you have the T in the daughter it is actually going to start synthesizing the A and as a result what will happen is that wherever you have in the G it is going to be replaced by A. So it is actually going to have the G to A mutations and if you have G to A mutations then it is actually going to change many things it is going to change the amino acid what is corresponding to the G to A substitution and so on. And then you have the substitution mutations so and during replication itself to the substitution mutation or the frame shift mutations.

So substitution of one base pair into another is called as a substitution mutation the swapping of the base pair may be a transition mutation or the transversal mutations. So what is the transition mutations? Subsolution of one pyrimidine by another pyrimidine or one purine by another purine is called as the transition mutations. For example G to C is going to be replaced by A and T and vice versa. So in that case it is actually going to cause the substitution mutations. Then you have the transversion mutations so purine is replaced by the pyrimidine or the pyrimidine is replaced by the purine.

So subsequent transversion is transition for example G to A or A to G or C to T or T to C. These are the if the G is replaced by A then it is going to be called as transition mutations or A is replaced by G then it is also going to be called because the pyrimidine is replaced by the pyrimidine and purine is replaced by the purine. But if it is the

pyrimidine which is replaced by the purine then it is going to be called as transversal. So both of these kind of substitutions are actually going to be very very problematic because it is going to overall change the amino acids and it is going to cause the mutations into the subsequent gene products. Then you have the frame shift mutations.

So sometime it may happen that during the application some extra nucleotide may get inserted or may get may not get copied. So you can actually have the either the addition of the extra nucleotides or you can actually have the disappearance or the deletion of some of the mutations and in both of these cases there it is actually going to cause the frame shift mutation. This frame information anyway you will be able to understand when we are going to discuss about the translation because you know that the protein is going to be synthesized in the form of the codons and codon is made up of the 3 nucleotides. So protein is been synthesized in the form of the codon. So for example this is the codon ATG.

So this 3 nucleotides are going to be read together by the anti codon what is present onto the tRNA. But now imagine that if I add one more A into this so what will happen is it is going to be a this sequence. Now if I go by the 3 triplicates then it is actually going to be like this. This means earlier the codon was ATG now the codon is going to be ATA and codon for ATG is going to be X amino acid whereas codon for ATA could be Y amino acid and that is how there could be a change in the amino acid what is going to be incorporated into the protein. The another example is that for example if I have the A here and if I or C for example.

So if I have a sequence like ATG C A and if I remove actually if I remove for example if I remove this actually. So if I there will be a deletion then what will happen is it is going to have this. So earlier you are having this as a codon now you are going to have this as a codon. So this also is going to be cause of deletion. So this is going to happen because of the deletion this is going to happen because of the So if this happen in the exorheic region of DNA that may mainly change the translational reading frame has results in the production of a non functional protein which can be observed in a phenotypic characteristics.

So it is not only going to change the codon for this it is actually going to change the codon for subsequent generation also. For example it is going to change the frame shift rotation. So it is actually going to change the codon for example earlier you are having this. So this is the first codon this is the second codon. Now when you have removal of this G this G remove if you remove this T then you are going to have the first codon as AGC and the second codon would be ATT whereas earlier it was ATG and CAT.

So this was the codon. So this is not only going to change the frame shift only for first codon but also for the all the codons and because of that it is actually going to cause a significant change into the amino acid composition of the product and as a result it is actually going to change produce the protein which may not be functional and which may actually cause the problem to the cell. For example this is the example what is being given you have this is the standard frames what is present and when you have the mutations or messenger RNA what is going to be formed it is actually going to form but if you have the addition of T base pair then it is actually going to change. It is going to change the frames and that is how it is actually going to form the different mutations or if suppose you have the deletion then also you are going to change the things. So these are the some of the things which are very very important and the frame shift mutation is very very significant problems and as a result this shift to change in a translational reading frame hence name as the frame shift mutations. Then we have the second thing is spontaneous lesions naturally occurring damage to the DNA is called as the spontaneous lesions most common lesions are deaminations and depurinations.

So deaminations the loss of exonucleic amino acid group from the cytosine and adenine and the guanine due to change in the pH in temperature is spontaneously resulting in the formation of the uracil, hypoxanthine, xanthine and thymine respectively. So deamination is going to change the amino acid for example if there will be a deamination from these of the from of these nucleotides then it is actually going to be get converted into uracil, hypoxanthine, xanthine and thymine and that is actually going to result into the change in the structure or change in the nucleotide sequences. Then depurinations and depurimidations loss of purines and pyrimidine by the breakdown of the glossary bond nucleotide from the DNA due to damage due to the change in the pH and then you also going to have the oxidative damage, damage in the DNA due to the reactive species spontaneously radicals like peroxide, hydrogen peroxide and hoxadoxy radicals attacks on the DNA probe product reduce variety of products attack at several several leads to the fragments base loss and the strand streaks. So all of these things can also lead to the frame shift mutations and the spontaneous mutations as well. So these are the some of the example if you have the deaminations the cytosone is going to be get converted into uracil if there will be a deamination into the iodine it is actually going to be get converted into the hypoxanthine and then if you have the 5 methyl cytosine and if there will be a deamination it is going to be get converted into the thymine and if there will be a deamination into the guanine then it is actually going to be get converted into xanthine and some of these are non natural nucleotides so they will actually going to cause the significant mutations into the DNA structures.

And then we have the transpositions transposon is a DNA segment that have the capacity to insert itself at any location in the genome without having any relation to the

target sequence consequently it cause loss of gene fraction or genes inappropriate over expressions. So transposition is a very important and the very significant topic that you should actually study and transposons are also called as the jumping genes and they are actually changing its position from the one locus of the genome to the another locus and as a result they are actually causing the different types of artifacts and different types of problem into the genes. So they are actually going to cause the gene loss of gene functions or genes appropriate over expressions. So transposon is a very important and the big topic so that you can actually be if you are interested you can be able to study this from any of the standard another molecular biology books. And then we have the induced mutations.

So mutagens results into the induced mutations mutagens can be classified as a physical mutagens and the chemical mutagens. So these are the physical mutagens where you have the UV radiations, ionizing radiations and the heat. So UV radiations UV radiation is a potent physical agent that cause a number of photo photo product in the DNA. UV radiation of the wavelength 260 nanometer induced dimerization of the pyrimidine nucleotides bases especially thymine resulting in the formation of the cyclobutyl dimers. So this is what exactly happened when you have the two nucleotide they will be getting exposed to the UV they are actually going to get dimerized and they are actually going to form the cyclobutene rings.

Adjacent pyrimidines are covalently linked to the formation of four member ring structure and this structure is called as the pyrimidine dimers. Then ionizing radiation mainly causes the DNA strand breakage and then you also have the heat stimulate the wave induced cleavage of the N glycosidic bond which result in the apirenic or apiremitinic side or the baseless sides. So in this particular thing what will happen is that there will be a cleavage of the glycosidic bond and you know that the glycosidic bond is holding the sugar to the base and because of that there will be no base what is present on to these particular nucleotides. Then we have the chemical mutagens so in the chemical mutagens you can have the four categories the base analogs, de-animating agents, alkylating agents and the intercalating agents. Base analogs are certain bases which are not present in the DNA normally but resembles to the normal nitrogenous bases that can incorporate during the DNA synthesis.

For example the 5 bromo uracil which was base analog to the thiamine and the 2 amino purine which is analog of the adenine. So these are the base analogs are going to induce the mutations because they are going to mimic the natural bases but they are not the natural and they will be get incorporated into the DNA during the DNA synthesis. Then we have the de-animating agents which causes the point mutation by removal of the amino group from the nitrogenous bases. Nitrous acid de-aminate the adenine, cytosine

and guanine. Then bisulfite de-aminate only cytosine and the de-amination of adenine give rise to the hypoxanthine which pair with C instead of T and de-amination of cytosine give rise to uracil which pairs with A instead of G and this actually is going to cause the problem into the first generation and as well as into subsequent generation because of the C to T mutations and A to G mutations.

Then we have the alkylating agents so some example of alkylating agents are like ethylene methane sulfone or the nitrogen mustard and the dimethyl nitrosamine. These agents actually add the alkyl group to the certain position in the nucleotide and these alkylating agents are not is actually going to cause the mutation and that is why it is actually going to kill the cells. Many of the anti-cancer drugs are also alkylating agents so they alkylate the DNA and that is how they are actually activating the machinery to you know to kill these cells. And then we have intercalating agents usually associated with the simple single mutation pair insertion or deletions. Intercalating agents are flat molecule that flip between the base pair in the double helix resulting into the unwinding of the DNA helix and therefore increasing distance between the adjacent base pairs.

Some examples are proflavine, acridine orange, ethidium bromide and the ICR compounds. Intercalating agent is also very, very problematic because they were going to interfere into the DNA synthesis and they are also going to change the normal DNA structures and that is how they are actually going to cause the mutations. So these are the one of the effects by which the so for example, if this is the DNA, how the base analog is actually causing the problem. So for example, this is the normal DNA and you have the A which is and in the template in the corresponding template you are going to have T. Now, if there will be a base mutation, so example the 5 bromo uracil is going to be present inside of A, then the BU is actually going to so if there will be a BU undergoes tautomeric shift then BU is actually going to get converted into this and that is how it is actually going to have the interaction, it is going to have the affinity for the C rather than G because this is going to have the affinity for G rather than C, rather than A because A U should have an affinity for A, but it does not have the affinity for A, it has the affinity for G.

So, instead of so what will happen is when the replication occurs in the wild type the A is going to form and A is going to be synthesized instead of in front of T, but in this one instead of this you are going to have the G. Now, once you do the another round of applications A this wild type will not actually have any problem because it is going to still have the A to T, but here now the G is first mutated and now the second strand is also going to be mutated and that is how it is actually going to have the C. So, this is actually going to be a mutated DNA what is going to be formed and this mutated DNA if you do the subsequent mutations subsequent replications will proliferate and it will

continue into the subsequent cells actually or notodotus cells. Similarly you may have the deaminating agents for example, adenine when it is going to be attached to the nitrous acid it is going to get converted into hypoxanthine or the cytosine when it is going to get converted into AT. So, once you have the adenine to the hypoxanthine, hypoxanthine will not going to form the interaction with T instead it is actually going to have the interaction with C and because of this the AT is actually going to be replaced by GC exactly with the same mechanism that in the first generation the A will actually going to recognize the T, but in the subsequent generation when the A will get converted as hypoxanthine the daughter strand is going to have the cytosine and cytosine is actually going to incorporate the C.

So, that is what exactly going to happen in the subsequent generation in with the deaminating agents and then you also going to have the alkylating agent for example, guanine is going to get converted into the ethylene guanine and ethylene guanine is going to have the affinity for thymine instead of the interaction for cytosine and because of that there will be a reverse. In this case the AT is being replaced by GC in this case the GC is going to replace by AT and the same is true for the thymine when it is getting alkylated it is going to form the ethylene thymine and ethylene thymine have a interaction or going to make the base pairing with the guanine rather than the adenine and as a result the TA is going to replace by the CG. So, these are the some of the mechanism through which the DNA is going to be mutated. Now how the DNA if the DNA got damaged whether it is going to be damaged by the spontaneous mutations or it is going to be damaged by the induced mutations you are supposed to repair these changes. But supposed to have the machinery to detect and then if possible you can actually be able to have the repairing of these things.

So systems for repairing the numerous unintended lesion that frequently occurs in DNA are also required for maintaining the genetic stability in addition to the extremely precise DNA replication mechanism. The vast majority of these unintentional DNA replications are temporary because the DNA repair a group of connected system immediately correct them. Without repair processes a genome cannot maintain its essential biological functions. These DNA repair mechanism fall into the two broad categories direct reversal of the chemical process that cause the DNA damage and the damage bases are removed and then replaced with the freshly synthesized DNA. So you have the two choices of you know reversing these damages.

First you can actually be able to reverse the process you can actually reverse the reaction for example if you have the alkylating agents you can actually reverse the alkylating agent and you know reverse these reactions so that the guanine is going to be converted into back to the adenine and so on. Another thing is that you can just replace

these damaged base and replace it with the normal base and that is also going to be another base. So additional mechanism have developed to help the cell deal with the damage where the DNA repair fails. DNA repair mechanisms you can actually have the single stand break repair mechanism or the double standard break mechanism. In the single stand break mechanism you can have the direct reversal, excisions, mismatched repairs and within the excision repairs you can have the nucleotide excision repairs or the base excision repairs.

Whereas in the double strand breaks you can have the homologous recombination or the non homologous DNA recombination. So single stand breaks you can have the direct reversal so directly acting on the damaged nucleotide converting back to the original structures. So pyrimidine dimers are usually repaired by a light dependent direct reversal process called as the photo reactivations. DNA photolyase enzyme participate in the mechanism which is found into the E. coli these enzyme get activated with the wavelength of the 300 nanometer and the 500 nanometer the enzyme binds to the pyrimidine dimer and convert back to the original monomeric and nucleotides.

So this is what exactly happened when you have the thymine dimers which are going to be formed and when you are exposing this particular DNA with a visible light it is actually going to have the photolyases of this particular strands where you are actually having the nucleotide dimer which is being formed. And then with the help of the enzyme which is called as the DNA photolyase it is actually going to replaced and it is going to remove these nucleotides and it is going to form the normal DNA. So these are going to reversed and that is how it is actually going to recover the DNA. Then we also have the excision repairs so excision repairs it involves the excision of the damaged segment of DNA followed by the re-synthesis of the current nucleotide sequence by an enzyme which is called as DNA polymerase. So base excision repairs you can actually have the removal of the damaged base used to repair minor damages like the alkylation, deamination which are consequence of exposure to the mutagens.

It is initiated by enzyme which is called as DNA glycosylase and the DNA glycosylase cleaved at glycosidic linkage and detaching the altered base as a result an a-pyrenic or a-pyramidinic sites are generated. Final ligation of the nucleotide take place by the DNA polymerase and the DNA ligase. So these are the this is the mechanism where you are actually having the UDG role of the UDG uracilidin and glycosylase. So if you have the deaminated cytosine which is actually going to be uracil and that is actually going to first form the a-pyrenic sites and then this a-pyrenic sites are actually going to refilled back and that is how you are going to have the repaired DNA at the end of this particular repairing mechanisms.

Then you can also have the nucleotide excision repairs. So similar to base excision repair it acts on a more substantially damage area on the DNA it include the following steps. So damaged DNA first you are going to have the damaged DNA the breakage of the phosphodiester bond on the either side of the damaged portion. So for example this is the damaged DNA so on the both side you are going to have the breakage of the phosphodiester bond and then you are going to have the excision leaves gap. So you are going to have a gap which is going to be created and this gap is going to be filled by the DNA polymerase and ligase seal the breaks. The best studies mechanism for the DNA replays is the UVR system into the E.

coli a key enzyme is involved called ABC exonuclease which is made up of the three subunit UVR A, UVR B and UVR C genes and ABC XC nucleus binds to the damaged site on the DNA and cut the phosphodiester bond on the both 5 prime and 3 prime. UVR D is acting as a helix case and helps to unwind the DNA at the site of the cut the gap is filled by the DNA polymerase one and sealed by the ligase. And then we have the third mechanism the third mechanism is called as a mismatch repair. It detects the mismatch that occurs during the renin applications. The mismatch repair occurs in daughter strand and it highly prone to the mismatch during the replications.

How to distinguish between the parent strand and the daughter strands? Immediately after the replication parent strand will be containing methyl group whereas the daughter strand await for the introduction of the methyl group. In this way the two strand can be distinguished and this is the best time period for the repair mechanism to scan the lesion like the correction. So this is very important that see the damage will only going to occur into the daughter cells rather than the parent cell. So parent cell you are just remove going to remain as intact in the daughter cells you are going to have these kind of repair mechanisms. And how you are going to recognize the daughter cell the daughter DNA the daughter DNA is going to be unmethylated because the methylation still not been done for all the adenine groups.

How the methylation occurs? In E. coli the methylation is executed by an enzyme which is called as the DNA adenine methylase which converts the adenosine to the 6 methyl adenosine in the sequence sequences like GATC and the DNA cytosine methylase which converts cytosine into the 5 methyl cytosine in the 5 prime sequences. It should be noted that these methylations are not mutagenic the modified version have the same base property as the unmodified one. And then E. coli the mechanism is completed by the mut protein there is a involvement of 3 mut proteins the mutH mutL and mutS mutH and mutL recognize the sequence GATC and mismatch respectively. And then we also have the SOS response so sometime a DNA damage is so dangerous that is stimulate the cells to produce the DNA repair enzyme that allows an immediate

reaction to the specific DNA damage.

SOS response in bacteria is the most well researched illustrations when the bacterial chromosome is severely damaged the SOS response genes are activated many of these genes are involved in a repair and mutagenesis. Rekia protein and LexA repressors are the main player in the SOS response. LexA is a repressor that point to the 20 base pair segment of DNA known as SOS box to prevent the activation of the SOS response genes. As a result the LexA govern the transcription of the edge each SOS response genes. So this is just a mechanism through which the SOS response is happening the three you are going to have the SOS box where the LexA gene is going to bind and that is how it is going to start the SOS response gene transcription.

And there will be no transcription if the of the SOS response so there will be no damage into the chromosomal DNA. But if there will be a damage into the chromosomal DNA then the is lekA you are going to have the recruitment of rekA and that is how it is actually going to cause the cleavage of the LexA and once there will be a cleavage of LexA then this inhibition or the attenuation is going to be removed and that is how the SOS box is free and that is how it is actually going to cause the production of the SOS response gene and that is actually going to cause the bacterial chromosome damage repairing. And then we also have the double strand breaks so far what we have discussing we were discussing about the single stranded break repair mechanisms. In the double standard break mechanisms you have the two mechanisms the homologous recombinations and the other kinds of mechanisms. So these are the some of the steps what you are supposed to follow when you are going to have the homologous recombinations.

And these steps are very very important and we are going to discuss in detail of all these steps when we are going to discuss about the genome editing and other kinds of phenomena in a subsequent lectures. And then we are going to have the non homologous DNA repair and joining and all these we are actually going to discuss because the non homologous process repair double standard breaks in the DNA and this process is known as homologous because of the break DNA are directly ligated without any homologous template. Term was pointed by the Maury and Haber in the year of 1996 and double standard breaks are recognized by a protein which is called as Ku 70 by 80 and the Ku 70 by 80 recruit the DNA pks or the kinases and is then recruit the Artemis which remove the damaged ends. So in conclusion DNA damage is inevitable due to the various factors cells have evolved DNA repair mechanism to counteract the DNA damage. Types of DNA damage includes the breaks, base modification and cross links repair pathway like the burner, MMR and HR fix the different type of DNA damages.

Accumulated unrepaired DNA damage can lead to the mutation and disease including the cancers. Nerve repair mechanism contribute to the cancer development. Some cancer therapies exploit the DNA repair mechanisms and that is how they can actually cause the mutations into the cancer cells and since you are going to have several mutations the cancer cell will have no option but to die actually. Aging is linked to the declining DNA repair efficiency the environmental factor can overwhelm the DNA repair mechanisms and ongoing research are seek to improve the understanding and develop the therapies. So there are many mechanism the DNA once the DNA is damaged there will be many mechanism through which the DNA is been repaired into the eukaryotic cell or the prokaryotic cell.

So this is all about the DNA damage and repair mechanisms and we have discussed various mutagenic molecules which are actually causing the induced mutations. We have also discussed about the spontaneous mutations and how the spontaneous mutation is happening because of the error prone because of the DNA replications and the other phenomena. So with this I would like to conclude my lecture here and subsequent lecture we are going to discuss some more aspects related to molecular biology. Thank you. Thank you.