DNA Mutations

So the question is what is the significance of DNA mutations? What do they mean? How are they involved in evolution? What's the difference between a neutral and a benign mutation and a harmful mutation? So basically mutations are random changes that happen to the amino acid structure of the gene. They can also happen to different areas, but they can involve many different processes. They could involve large parts of genes that can be deleted. Parts of genes can be copied and not copied properly. You can get the common single nucleotide mutation where just one base pair gets changed. What happens there is, you'll have an error in the copying process. What happens is a piece of DNA can get damaged and then the cell will fill in any sort of base pair it assumes is going to be the right one if it doesn't have a template to copy it from.

Let's say you have a piece of DNA that's damaged. The cell goes to copy itself and it runs into this damage. Think of it as a highway with a bridge out. Normally the cell will use the other strand of the DNA. There's two strands of DNA. Normally we'll use the other strand to determine what is supposed to be there, but in some cases, the DNA mutation can happen to both strands.

Then the cell doesn't know what to do. So what it will do is it will do something called the error prone pathway. Basically all this is, is it says, well, we don't know what's supposed to go here so we're just going to put a C or a G nucleotide and hope that that that's the right one and it fixes it.

So then the cell cycle we'll go through the whole cycle. If it doesn't recognize that this is a mutation, or this is not the right base pair, then what it will do is allow the cell to reproduce. S o once the cell is reproduced and it has this new base pair in there, that's thrown in just to fix the damage; then that is referred to as a mutation. So a mutation is what occurs once the DNA repair process has already gone through its stages and i t's a failed DNA repair process. Normally, if the cell recognizes this mutation, it will stop the cell from reproducing. When you get a mutation, the cell cycle is not stopped and the mutation gets incorporated into the new DNA of the new cell. Now this happens on a daily basis and our body has many different ways of dealing with this.

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We have a large genome with lots of what we call junk DNA, which is not really junk. It acts as a backpack for fixing and altering, different genes. I n the case of a mutation, if you have this mutation in a specific gene, if it doesn't change the amino acid structure, then it's considered benign. So I'll just back up the bus a little bit. What happens is there is three different base pairs that encode for amino acid, but there's a certain amount of redundancy. So you can change a couple of those base pairs and still get the same amino acid coding. So in other words, one amino acid coding has multiple different three base pair combinations that can create that same amino acids. So there's some functional redundancy there.

Not every mutation is going to cause a change to that amino acid . If it does cause a change in the amino acid , potentially it's either going to be a beneficial mutation that increases the fitness of the gene and increases the fitness of the individual, or it's going to be a damaging mutation. So benign mutation means it doesn't change the, structure and the same amino acid is put there regardless that this base pair has changed. That would be a neutral, benign mutation. If it causes a change of an amino acid that is very similar to what is supposed to be there, then it can also be a somewhat benign mutation. If it increases the fitness of the individual then it's a positive mutation a nd that's about evolution.

Evolution is a very slow process and the vast majority of mutations that occur are not going to improve the fitness of the species. A lot of them are neutral. The vast majority of mutations are neutral, benign. A harmful mutation occurs when it changes the three-dimensional and the four dimensional structure of the protein. T here's lots of different biochemical and bio- electrical charges that dictate which amino acids attached to each other and form three-dimensional structure or four-dimensional structure. If that changes, then that particular protein or gene product will not have the same function. It will fit into different receptors or will change how it attaches to the receptor. In the case of cancer, if it happens in an onco gene, it will change the amino acid structure. You'll get a different amino acid at a position and then that amino acid will change the structure of the gene.

So the gene will get attached to its receptor and be unable to release. That's called constitutive activation or it will increase the amount of the gene product, depending where it happens. If it happens in a tumor suppressor gene, then what happens is it can prevent that tumor suppressor from performing its function. Most tumor suppressors are involved in repairing damage to DNA and preventing cells with mutations from coping themselves. Then you can have this process where a cell has a mutation but it's allowed to copy itself because the tumor suppressor genes involved in preventing that from happening are damaged. A common example is, the BRCA1 and 2 genes.