Genetic Engineering: Theory & Applications
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Module XI
Biotechnology in Social Welfare
Lecture 36
Applications of Biotechnology Part II

Hello, everybody this is Doctor Vishal Trivedi form department of bioscience and bioengineering IIT Guwahati. And, in the previous lecture what we discussed we have discussed about the applications of biotechnology in the agricultural science. In that lecture we discussed about how the genetic engineering as well as the biotechnology is allowing to generate the different types of plants species which are resistance for the disease as well as resistance for the abiotic stress. And all this advances have improved the crop production as well as they have increased the yield from the same plants. Now, in today's lecture we are going to discuss about the role of biotechnology in the animal sciences.

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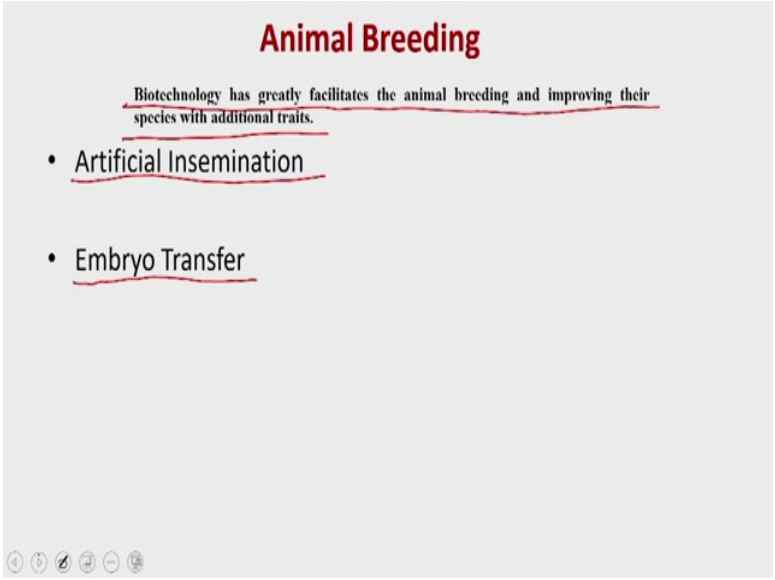

So, animal science, within the animal sciences what we are going to discuss about the role of biotechnology in the animal breeding. And, within the animal breeding the biotechnology has greatly facilitated the animal breeding and improving their species with additional traits, by discovering as well as validating the 2 processes. One is called artificial insemination the other one is called as the embryo transfer. And are both of this process are having its own significance, its own importance in the whole processes of animal breeding as well as improving the particular species with the desirable traits.

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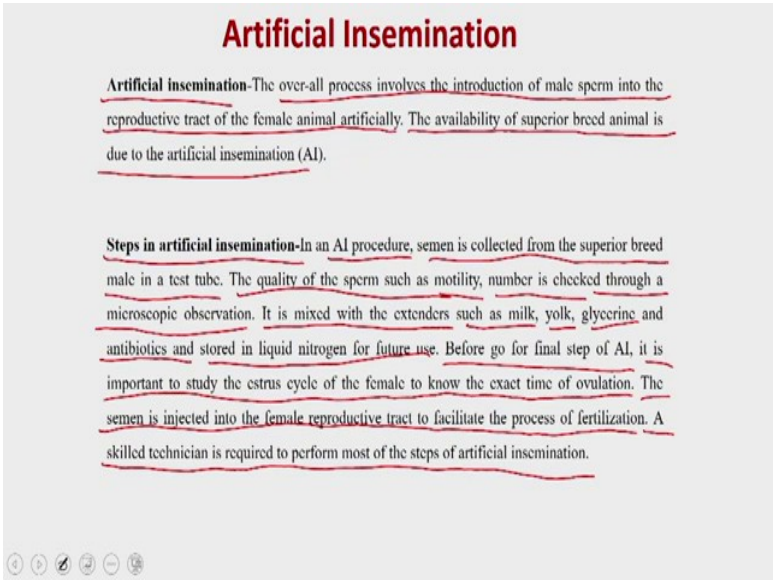

So, in the artificial inseminations the overall process involves introduction of male's sperms into the reproductive tracts of the female animal artificially. The availability of superior breed animal is due to the artificial inseminations. So, there are multiples steps which are involved in artificial inseminations. In an artificial inseminations procedure, the semen is collected from the superior breed male in a test tube. The quality of the sperm such as the mortality, the number of sperms in the semen is checked through microscopic observations.

And, then it is mixed with the extenders such as milk, yolk, glycerin as well as the antibiotics and in stored in a liquid nitrogen for future use. Now, before you go for the artificial inseminations it is important to study the estrus cycle of the female to know the exact time of ovulation. Because, it is important that you should know the estrus cycle of the receiving female counter part. So, that when you do the artificial inseminations the sperm what you are going to inject artificially are going to go and to the fertilizations. And that is how you are going to have the better traits with the help of this procedure. The semen is injected into the female reproductive tract to facilitate the process of fertilization. And because this is a very very difficult task skilled technician or the doctor is required to perform the most of the steps of artificial inseminations.

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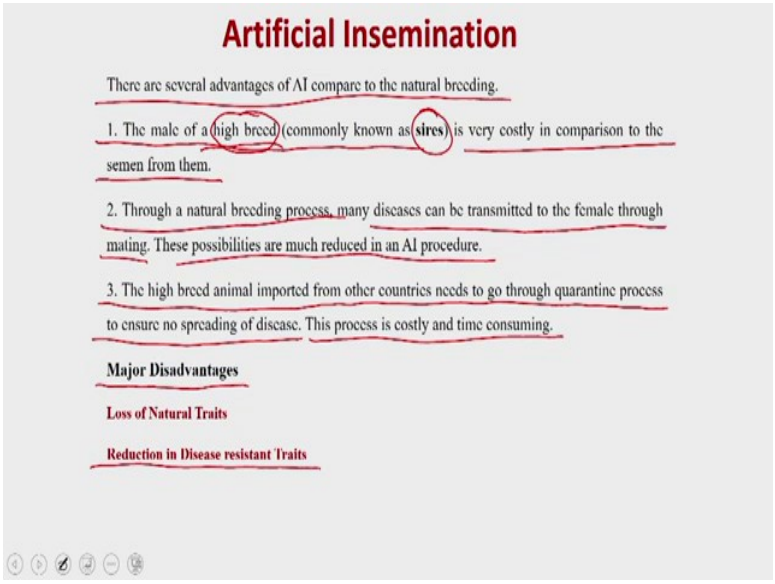

There are several advantages of artificial inseminations compare to the natural breeding. So, one of the major advantage of the artificial insemination compare to the natural breeding is that you could be able to introduce the desirable traits whichever you like to. So, in that case what have to do is the male of high breed which means the breed which is desirable, which is required for different types of proper process. For example, if you have to look for the breed which should very powerful in terms of using it for the agriculture purposes.

So, the breed what is going to be used for artificial inseminations is known as the sires and it is very costly in comparison to the semen from them. So, if you would like to buy the same breed from the same breed after it is going to be very costly, compared to that you buy the vial of semen from the same breed and that is going to be cheaper. So if you use the semen you are could be able to perform the artificial inseminations. And that is how actually you are going to get the similar breeds even in a, in this process as well.

Through a natural breeding process many disease can be transmitted to the female through mating. These possibilities are much reduced in an AI procedures. So, when people go for the natural breeding there are so many sexually transmitted disease which are going to go from the male to female during the fertilization steps. So, that kind of possibility can be reduced very significantly. Because, you can easily check the semen as well as the quality of sperm in a microscopic observation as well as we can perform many of the biochemical as well as the microbiological observation as well, to see if the semen is actually contaminated with any kind of the infectious organism or not.

The high breed animals imported from the other country need to go through a quarantine process to ensure no spreading of disease. So, what happen is when even if you would have a money and you would like to buy the high breed from the neighboring countries, when these breeds comes to our country they have to go for a quarantine process.

Quarantine is a process in which the animal is going to be kept in isolations and it has on also going to be under the observations. For the appearance of any kind of diseases what the animal is going to have. So, in the during this incubation procedures, the first of all the quarantine process is very costly. Because, the monitor the animal has to be monitor throughout these incubation periods and it actually so because, of that and it is also a time consuming process.

So, this process is very costly and time consuming. So, you have the 3 advantages first you can you do not have to go with the high breed animals, you can easily take up their semen and go for the artificial inseminations. So, with the help of the expert technicians you could be able to get the same breed. But, without going to the high cost of that particular breed. The number 2 is because you are using the artificial inseminations you could be able to control many of the sexually transmitted disease from the male to the female and so on.

And, the third is that you do not have to keep these animals under the quarantine process. So, you could be able to save the time as well as the money by following the artificial inseminations. But, there are major there are disadvantages of artificial inseminations. What are these advantages? See, we are living a country so we are having an inbreed spread inbreed animal species. And, the major advantage of this inbreed animal species, is that they are very resistances for the diseases which are occurring in our environment.

For example, if you are buying if you are going with the any kind of breed which is coming from Australia or America or Europe they have never been expose to these diseases. So, they are good in terms of the food milk productions, they may good in terms of their power, they may be good in many other traits. But, they may not be very good in terms of sustaining, the infectious organism what they are going to get in this environment. So, because these animals are never being kept in a tropical country like India.

They will never been acclimatized for this diseases. So, because of that the species what we are have which actually may not be good in terms of the economical point of view. But, they are very good in terms of the disease conditions or withstanding the environmental conditions. For example, our animals could be good in terms of withstanding very high

temperatures, very low temperatures and as well as very high quality of humidity. And, all this conditions are actually going to make the animals very sick in due course.

So, even if you go with the artificial inseminations you will keep going to get the high breeds which are going to give you the good milk productions they might be economically very happy. But, these animals may actually going to reduce the number of the natural breeders present in the vicinity. And, as a result if you reduce our animals in this course, you are actually going to lose the traits which are available in these animals and these traits are important, because, some of this traits might be very important in terms of providing the disease resistance. So, this is what you are going to lose the natural traits like the natural traits to combat the environmental conditions and as well as the natural traits to take care of the disease.

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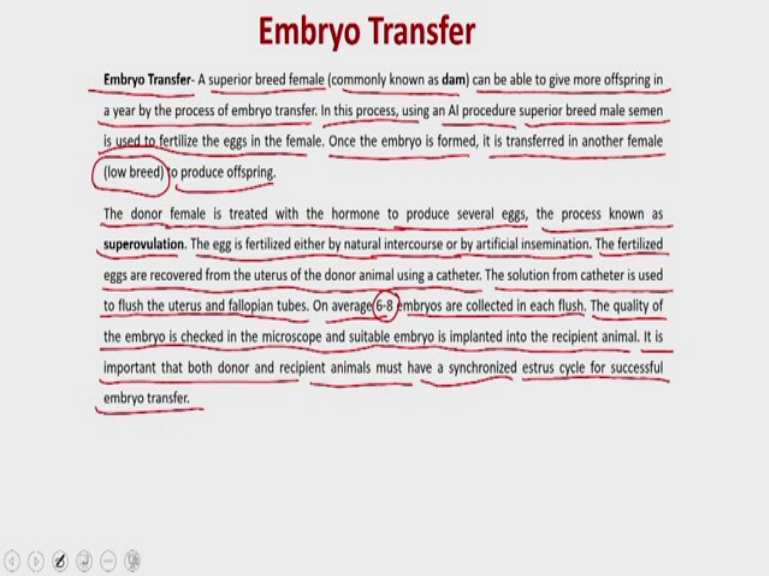

The second procedure is the Embryo Transfer so in the embryo transfer what you do is? You actually take a superior breed female normally known as dam and can be able to give the more offspring in a year by a process of embryo transfer. So, what will happen is you are actually having a superior breed female. But, a female has a limited number of babies which, it can actually produce in a single year. But, if you want to increase the productivity what you can do is you can generate the embryos in a superior female.

And, then what you can do is you can transfer these embryos to the another female and allow that female to develop the embryo. Because, what is more important is that the embryo is of a very high quality. So, have generated the embryo in a good quality or high breed female. And, then ultimately you have transferred this embryo into a low profile females. So, in this

process using an artificial inseminations superior breed male semen is used to fertilize the eggs in the female.

Once the embryo is formed, it is transferred to another female which is actually going to low breed. So, that you do not have to spend lot of money on keeping these females to produce the offsprings. The donor female so what is the procedure? The procedure is the donor female is treated with the variety of the hormones. So, that it will produce several eggs, the process known as the superovulations. The egg is fertilized either by the natural intercourse so, that you can allow the males to go for the fertilizations or you can go with the artificial inseminations.

The fertilized eggs are recovered from the uterus of the donor animal using a catheter. The solution from the catheter is used to flush the uterus and the fallopian tube. On average 6 to 8 embryos are collected in each flush. The quality of this embryos are going to be checked in the microscopy and then the suitable embryos are going to be implanted in to the recipient animal. It is important that both the donor as well as the recipient animal must have a synchronized estrus cycle for successful embryo transfer.

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So, if you see the procedure the procedure is very simple. First, of all what you are going to do is you are going to take the high breed female. You are going to inject the some of the gonadotropin hormones. And, once you inject the gonadotropin hormones what will happen is? It is going to start producing the eggs from the ovary. And, then either you go for the natural sexual intercourse or you can use the artificial inseminations after the superovulations. And, that artificial inseminations is going to create the embryos.

Now, what you have to do is in a non surgical recovery of this embryos after the insemination. So, you can take after 6 to 8 days after the inseminations you can recover these embryos. And, you can use the catheter which is called as Foley's catheter to recover these embryos from the superior females. And, then each embryo can be observed under the microscope for the classification of whether good quality embryos or the bad qualities embryos. Then you can segregate the good, or the bad quality embryos under the microscope.

And, these embryos can be stored in a liquid nitrogen either for the indefinite storage. Or, it can be stored in 37 degree Celsius or room temperature for 1 day. After this you what you have to do is you have to transfer the embryo to the recipient surgically or non surgically. So, you can do a surgery on to the recipient animal and you can implant these embryos into the uterus so that they will be going too developed. Then, you can actually detect the pregnancy by palpitations through the rectal wall after 1 to 3 months of the embryo transfer.

In this step you have to be ensure that the donor as well as the recipient females are going to be in a synchronize estrous cycle. So, that the hormonal profiling of the donor animal as well as the accepter animal are going to be same. Otherwise, in many cases what will happen is when you going to implant the embryos into the uterus. The female hormonal cycles are may not be in a conditions or you it may not be in a condition. So, that they will not accept the embryos and ultimately embryos are going to be remove from the uterus by the abortions.

So, that to avoid the abortion like conditions. We have to keep the donor as well as the acceptor in a synchronous estrous cycle so that the hormonal profiling should match with each other. Now, after the period of 9 months the embryos are going too developed into the calf. And, by following this embryo transfer methods or embryo transfer technologies, you can able to have multiple calf of high quality calf, from the same high breed animal. So, because you can actually have multiple recipients and these multiple recipients are going to give you the multiple calf in a signal year. Whereas, if you go with natural process the high breeder are going to give you only one calf in a single year.

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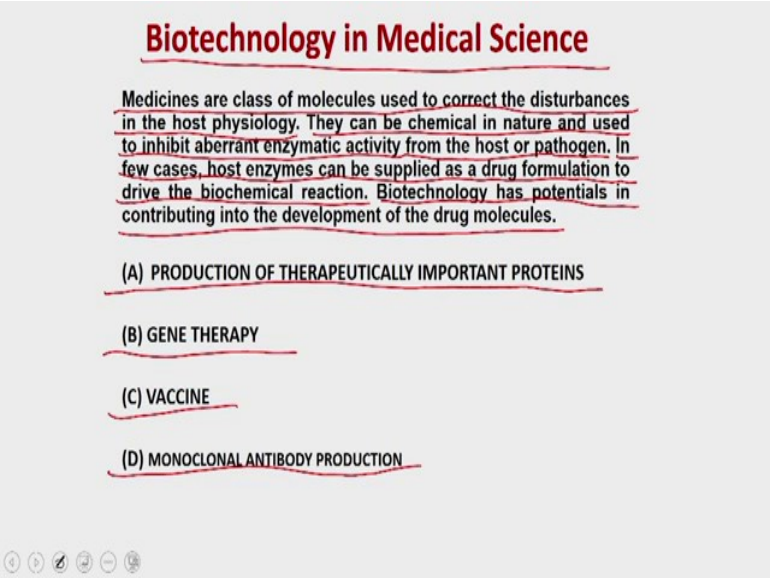

Now, let us go on to the role of biotechnology in the medical sciences. Though medicines are the class of molecules used to correct the disturbances in the host physiology. They can be chemical in nature to use to inhibit the aberrant enzymatic activity from the host, or they can be a chemical which going to be inhibit the activity in the pathogen. Both are this conditions are going to give you the normalcy in the in terms of the maintaining the inner homeostasis of the host.

In few cases host enzyme can be supplied as a drug formulations to drive the biochemical reactions. That is why the biochemical has the potentials in contributing into the development of the drug molecules. So, within the role of biotechnology in medical sciences we are going to discuss about the 4 aspects. What we are going to discuss? We are going to discuss about the production of therapeutically important proteins. We are going to discuss about the gene therapy, vaccines, and lastly we are going to discuss about the production of monoclonal antibodies and the role of biotechnology in these processes.

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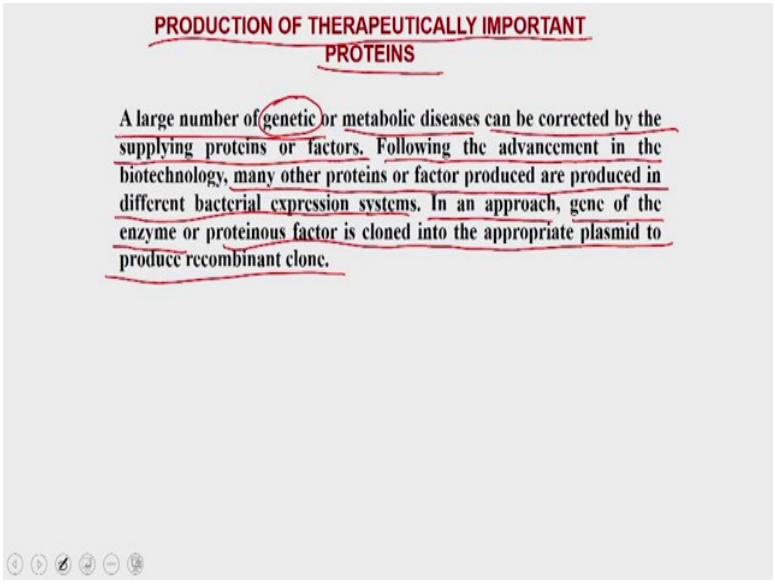

The production of therapeutically important proteins are large number of genetic or metabolic diseases can be corrected by the supplying protein or factor. So, you know that the human body or in general, you mean a single cell depends on the many of the metabolic reactions. And, all these metabolic reactions requires enzyme on the top, this metabolic reactions are controlled by the cell surface signalings. And, the cell surface signalings are in turn being regulated, by the different types of hormones which are going to be produced within the host.

So, there is a complex processes in which the host is actually making a fine balance about the different types of enzymes which are available in driving the metabolic reactions. The amount of enzyme the activity of the enzyme per say and so on. So, all these enzymes are important the hormones which are regulating these activities are very important. And, the combination of this 2 are actually going to be used to maintain a normalcy in host. What will happen is when you do not have any of this condition.

For example, because of genetic disease or because of the absence of an enzyme in a metabolic reactions, you are going to start developing the metabolic diseases or non-metabolic diseases. So, what will happen? If you want to correct this, you have to use the biotechnology principles. And, you can be able to provide this factor so what will happen if suppose you are genetically modified, or you are genetically mutant for a particular enzyme. Or at a particular stage of your life cycle you are actually being program in such a way, so that you will not going to produce that particular enzyme.

In both of this conditions you are going to develop the metabolic diseases. So, what you supposed to do is you are going to break the protein or factor you can produce in the bacterial

expression system. And, then you can supply these proteins from that particular system in a artificial way. Which means like you have to supplement these enzymes which are going to drive the metabolic reactions.

So, in this particular type of approach, the gene of that particular enzyme or the protein factor is cloned into the appropriate plasmid to produce the recombinant clone. And, these recombinant clones are going to give you these therapeutic proteins and then what you can do is, you can take these therapeutic proteins as a supplement to overcome this defects. Either it is genetic defects or the age dependent defects. For example, you might be producing the insulin when you are young but in due course when the age crosses the 40 or 50, you have start producing lesser and lesser amount of insulin in those cases use your body is requiring the insulin exogenously. So, that is why you are going to supply some amount of insulin which you are going to produce in a recombinant system. And, that is how you are going to overcome the deficiency which is being developed in your body.

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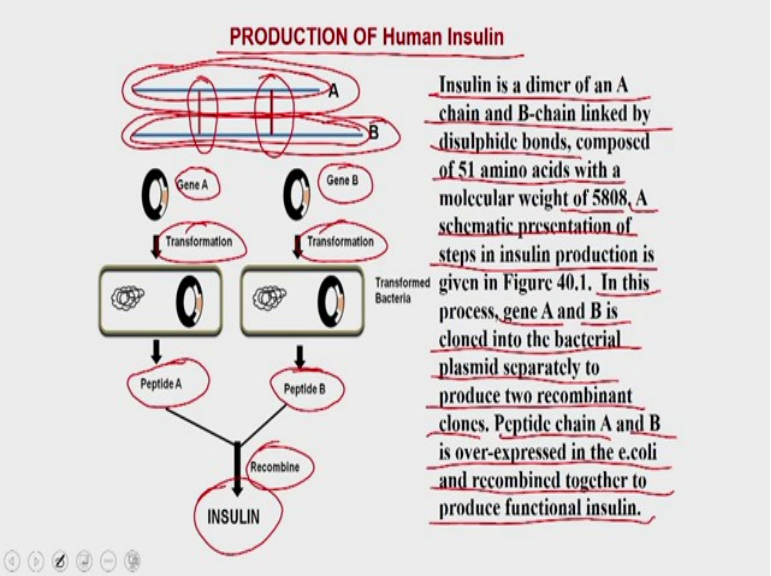

Now, let us take an example of the production of human insulin. So, insulin is a dimer of A chain and B chain which are linked by the disulphide bond. So, in an insulin you have 2 chain one is called A chain another one is called as B chain. And, both are this A and B chain are being produced separately. And, then they are being linked each other by the disulphide linkages, you have that two disulphide linkages between the A and the B chain. And, the molecular weight of an insulin is the 5808 Dalton.

And the total length total amino acid 51 amino acids are being present in the A chain and the B chain. So, what you can do actually is if, you want to produce the human insulin you have

to first clone the gene A which is corresponding to this peptide chain. Then you have to clone the gene B in a separate clone which is going to give you this peptide. And, then what you do is you transform the gene A as well as gene B containing recombinant DNA in to the bacteria.

And, then once you do that you are actually going to induce the bacteria and you are going to produce the proteins. So, the bacteria is going to give you and then you will purify so actually it is going to give the peptide A whereas, the other one is going to give the peptide B. And, then what you do is you take the peptide A and peptide B you recombine and that is how you are going to have the insulin at the end. So, in a schematic representation what you are going to do is in the insulin production is that in this process the gene A and the B is clone into a bacterial plasmid separately to produce the 2 recombinant clones. Peptide chain A and peptide B is over expressed in the E.coli and the recombined together to produce functional insulin. So, this is just the simple example to say that how the insulin or human insulin can be produced. In a recombinant expression system and that is how can be able to take this insulin to reduce the amount of insulin which your body is not being able to produce.

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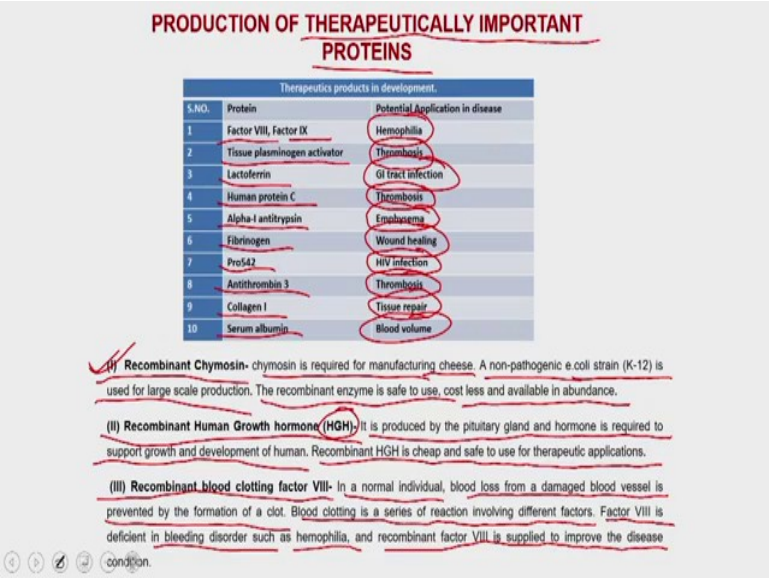

We have many the list of the therapeutic proteins which are being produced and which are going to be which are being in circulations to be used for overcoming the disease is conditions is very exhaustive. This is a simple list with the classical examples, so what you have is the factor 8 and factor 9. Both are these factors are required for the blood clotting so they are going to work in the case of hemophilia. Then, you have the tissue plasminogen activator which is actually is also going to work in the case of thrombosis.

Then you have the lactoferrin, lactoferrin is going to work in the case of Gi tract infections. Then you have the human protein C which is also to play a crucial role in the place of thrombosis. So, and then we have the alpha I antitrypsin which is actually is been used in the emphysema. Then you have the fibrinogen, fibrinogen is actually required for the blood clotting so that you have to use for wound healing. Then you have the Pro542 which is actually required for the HIV infections.

Then you have the antithrombin 3 which is actually required for the thrombosis. Then you have the collagen 1 which is actually requires for the tissue repair. And, then you have the serum albumin which is required for maintaining the constant volume of the blood. There are few examples I have taken these are called recombinant chymosin. So, chymosin is required for manufacturing the cheese, a nonpathogenic E. coli strain K12 is used to use for the large scale productions the recombinant enzyme is safe to use, cost less and available in abundances.

So, a part from the making a therapeutically important protein, you can also use or you can also produce the enzymes which is also very good in terms of economical uses. So, the recombinant chymosin is one of such example. Then we have the recombinant human growth hormone so, recombinant human grown hormone or HGH it is produce by the pituitary gland. And, hormone is required to support the growth and development of human. Recombinant HGH is cheap and safe to use for therapeutic applications.

Then the third is recombinant blood clotting factor number 8. In a normal individual blood loss from a damage blood vessel is prevented by the formation of a clot. The blood clotting is a series of reaction involving different factors. The factor 8 is deficient in bleeding the disorder such as hemophilia and recombinant factor 8 is going to supply to over some the diseases conditions. So, what happen in hemophilia is that suppose you got the injury you in a spontaneous process you are actually going to activate either the intrinsic pathway or extrinsic pathway.

And intrinsic or the extrinsic pathways are actually a series of cascades where you have multiple enzymes and ultimately these enzymes are terminating to the activation of thrombin. And, then once the thrombin is activated it is actually cutting the fibrogen. And, that once you cut the fibrogen you actually generates the fibrin. And these fibrin fibers are actually covering the clot or covering the wound and that is how you actually stopping the blood clot.

But, in this kind of disease conditions one or other factor is missing. And, as a result what will happen is that you are not going to be able to either complete this blood clotting cascades. Or, even if you will be able to complete the reaction may not be that efficient so because that you are going to lose lot of blood from the wound. And, as a result the person is going to be it could be life threatening conditions where the person may not be able to stop its blood clotting or stop the blood from the wound. And, as a result you are going to lose lot of blood.

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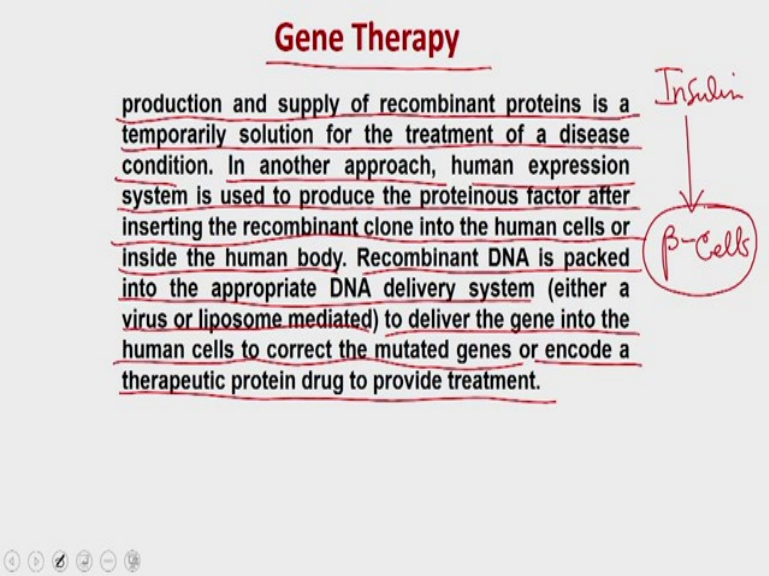

Now, gene therapy so the production whatever we have discuss so far is that you can produce and supply the recombinant protein. But, that is the temporary solution for a disease which is actually genetically modified. Which, means if I am genetically proven that I am not going to produce the insulin or if I am genetically if there is genetic defect that I can not be able to produce the factor 8. Then, even if I supply the factor 8 it is going to be a temporary situation.

Because, you do not know when you are going to get the injury, when you do not know when you are going to have the meal and also all thing. So, and then all the other hand you might have to carry this drugs along with you all the time. Why? Because, if there is a requirement you have to take this medicines or you might have to take this pretentious factors to execute the processes. Whereas, in the gene therapy approach what you can do is you can actually take the any gene and start expressing the protein in your body itself and that is what the procedure is called as the gene therapy.

So, these solutions are temporary for the treatment of a diseases conditions. So, alternative is that the human expression system can be used to produce the proteinaceous factor after

inserting the recombinant clone into the human cells or inside the human body. Recombinant DNA is packed into the appropriate DNA delivery system. Either a virus or a liposome mediated system to deliver the gene in to the human cell to correct the mutated gene or encode a therapeutic protein drug to provide treatment.

When you talk about the delivery it is also important that you do a delivery to a specific cell. For example, if you are talking about the insulin we have to deliver the cells we have to deliver this recombinant clone to the beta cell. Because, beta cells are the cells which are actually being trained to produce the insulin. We cannot produce the insulin in muscles or you cannot produce the insulin in brain.

Because, that is not the purpose of this cells because if you do so you are actually going to also interfere the metabolic reactions. Which are occurring in these cells as well as you are going to disturb the physiology of that particular organ. So, that is also very important that you actually not only going to translate the cells with the help of the viruses or the liposome. You also should do the targeted transformation or the targeted delivery of these recombinant clones.

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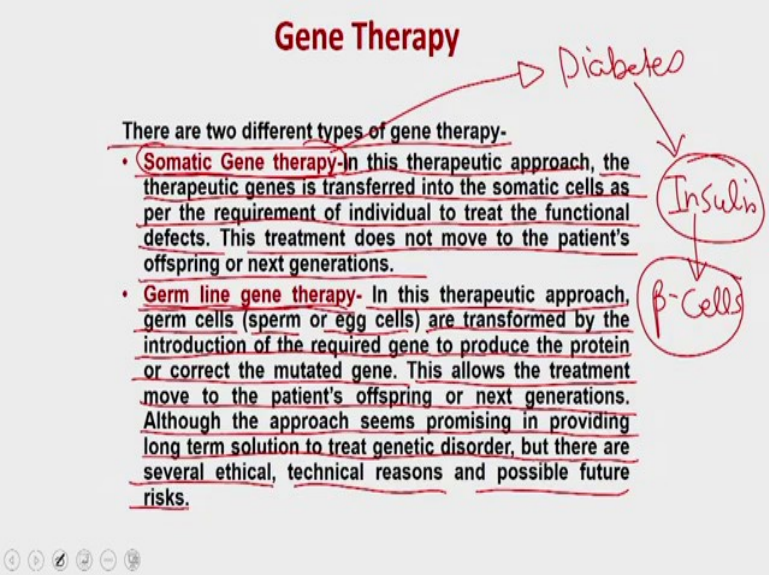

Gene therapy is of two types gene therapy could be of somatic gene therapy. So, somatic gene therapy is that in this therapeutic approach, the therapeutic genes is transferred into the somatic cells as per the requirement of the individual to treat the functional defects. This treatment does not move to the patient's offspring or next generation. For example, so the example of the somatic gene therapy is that the diabetes so if someone is suffering from diabetes because it cannot produce the insulin.

Then what you can do is, you can recombinantly clone the insulin A and B gene into a recombinant DNA and then you deliver that to the beta cells. But, so the advantage is that the that particular individual is going to start producing the insulin. But, this particular type of defects are not going to move to the next generation. Because, the transaction as well as the integration of this particular gene into the genome what you, which you have planned is going to happen only into the somatic cells.

It is not going to happen into the germ line cells which means this information is not present in the germ line cells so, it will not transfer from one generation to another generation. So, it will go into give you the permanent cure for that particular individual. But, it will not go to the as a cure to the offsprings. Whereas, in the germ line gene therapy in this therapeutic approach, the germ cells for example sperm or the egg cells are transformed by the introduction of the required gene to produce the protein or correct the mutated gene.

So, in some cases people are only having the mutation they do not have a problem of over expression or expression of this particular gene. They have a problem of that they have a mutated gene. So, in those cases you can actually can make the correct gene and then you can use the homologous recombination to replace this gene into the genome. And, that if you do that procedure into the cells or germ line. For example, if you do that procedure in sperm or ovum then it is once the embryo is going to form this information is going to replicate into the all cells of the offspring.

So, any kind of gene therapy when you do in the germ line it is going to propagate for the many generations. This allows the treatment move to the patient's offspring or to the next generation. Although, the approach seems promising in providing the long term solution to treat genetic disorder. But, there are several ethical technical reasons and possible future risks. So, it look very promising that you can use the gene therapy you can replace or you can do whatever kind of genetic manipulation of human beings. But it has lot of ethical issues, it has lot of social issues and it has and at the end it also has many of the technical obstacles to overcome and that is how the gene therapy also has many disadvantages.

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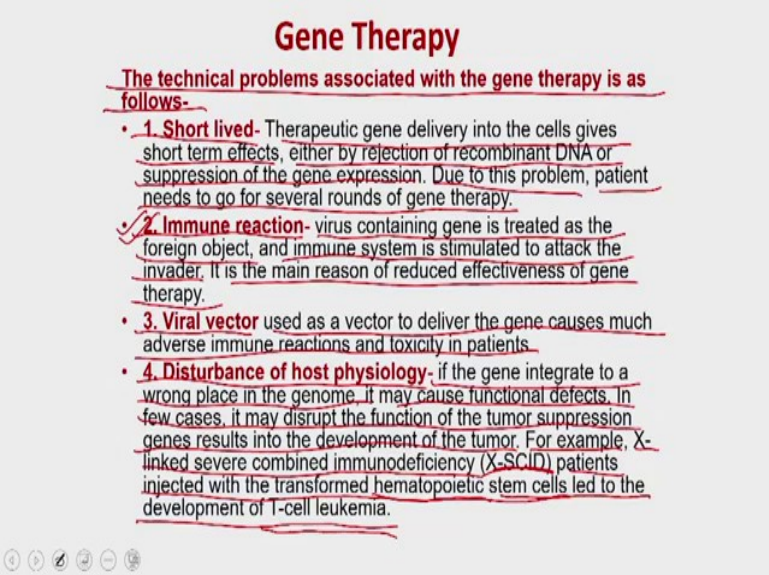

So, the technical problems associated with gene therapy is as follows. Number 1 it is short lived therapeutic gene delivery into the cells gives short term effects, either by rejection of recombinant DNA or suppression of the gene expression. Due to this problem, patients need to go for several rounds of gene therapy. So, what will happen is suppose you have given one round of injection to the patient and then the virus has gone to the beta cells it has started producing the insulin.

But in due course what will happen is because this are recombinant DNA the system does not may not actually accept this exogenous DNA. These cells are either this cells or the DNA itself is going to be short lived and because of that in due course the effect is going to be over. So, because of that you might have to need to have the multiple injections to maintain the level of protein productions. The second which is actually more serious is the immune reactions, the virus containing gene is treated as the foreign object, and immune system is stimulated to attack the invader.

It is the main reason of the reduce effectiveness of the gene therapy. So, this is actually a very very serious problem. Because, once you inject the virus containing genes into a human being the human body has a very pronounced or very good reliable immune system. So, these immune systems are going to recognize viruses as the foreign agent. And, because of that they will actually going to, either remove these viruses from the circulations or they will not allow these injected viruses to propagate and provide any kind of the long term effects.

Then the third the viral vectors, the viral vector is used to deliver the gene causes much adverse immune reactions and toxicity in patients. So, some of the people are very very

sensitive for virus as well as the viral derived products. And those people are going to show a severe anaphylactic shocks and sometime it may actually lead to the death of that particular individual as well. Number 4 the disturbance of host physiology, because whatever you are doing a exogenous thing it is actually going to disturb the human physiology.

So, if the gene integrate to a wrong place in the genome, it may cause functional defects. In few cases, it may disturb the function of the tumor suppression genes results into the development of the tumor. For example, x linked severe linked immunodeficiency X SCID patients injected with the transformed hematopoietic stem cells led to the development of the T cell leukemia. So, there are 2 things could happen one is that because you are actually putting an extra burden of the viruses, extra burden of recombinant DNA into the system. and as well as you are actually disturbing the metabolism by providing a exogenously supplied enzyme.

You are actually going to disturb the physiology of that particular individual. And, you know that the protein production from your recombinant DNA may not be having the same tight control compare to the naturally occurring the gene. So, because of that also you might be producing very large quantity of that particular protein or you might be producing very small or you may not be producing as per the requirements.

For example, if I need a hexokinase at time 0 or if need a hexokinase when I have taken a breakfast but, the hexokinase level might be very high even from the throughout the day. So, that actually is going to disturb the overall metabolism of that particular cell as well as the as an individual in totality. Other aspect is, suppose, the put the homologous sequences to these genes and ask them to go to recombinations. And if they will be any mistakes in this recombination process they may go and integrate into the genome and disturb the existing genes.

And because of that sometime what happen is they might be actually disturbing the tumor suppresser gene. So, if you actually going to remove the tumor suppresser gene from the system. You are spontaneously going to evolve, or you are spontaneously going to develop the large quantity of tumors. And, that is what exactly happens in the X-SCID patients if you take these X-SCID patients. And if you inject them with the hematopoietic stem cells they actually eventually develop the T cell leukemia. So, because of this kind of technical issues and because of this kind of problems so the gene therapy does not have any futures in terms

of providing the permanent solutions for the mutations. Or the deficiency in having the short supply of that particular recombinant factors.

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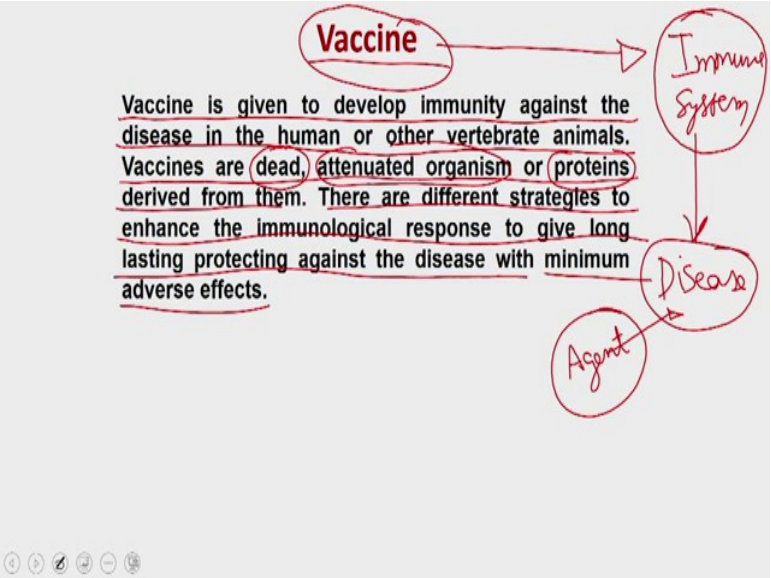

Now, let us move on to the vaccine so, vaccine is given to the develop immunity against the disease in the human or other vertebrate animals. Vaccines are of different types vaccines are dead, attenuated organism or proteins derived from them. There are different strategies to enhance the immunological responses to give long lasting protection against the disease with minimum adverse effects. So, vaccines are the molecule which are actually going to trained your immune system.

So, they are going to train your immune system so that your immune system is going to work against the particular disease. So, right now the disease causing agent may not be available, or may not be present in the host or present in the human being. But, once with the help of the vaccine you are actually training your immune system to combat the infectious disease cause by any kind of agent. Then, once this infectious disease agent comes it actually going to destroy this agent spontaneous.

So, it vaccine so the purpose of the vaccine is that it will go into give you the long term the immune response and that immune response is going to give you a, some kind of protection against this particular disease causing agents. And, in this case you can take the dead organisms, you can take the attenuated organisms or you can even take the proteins from that particular organism to challenge your immune system or you train your immune system in such a way that when the real organism is going to come. It is actually going to combat

against these infectious organisms and that is how they are going to eradicate this infectious organism from the system.

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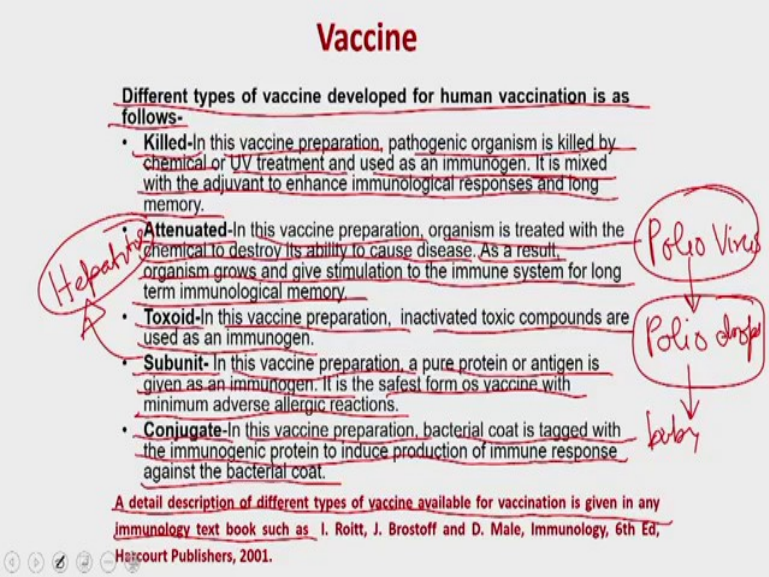

So, there are different types of vaccines which people have developed for vaccination. You have the killed vaccine, so in this vaccine preparation the pathogenic organism is killed by the chemical or the UV treatment and used as an immunogen. So, once you used these killed organisms as an immunogen it is actually going to increase your immunity against this particular infectious organism. This killed organism is mixed with the adjuvant to enhance the immunological responses and the long memory.

Which, means if you mix the killed organism with a adjuvant your actually not going to not only going to enhance the immunological responses, you are also going to generate lot of memory B cells. And, because of that if you are going to have the very long memory to combat against this particular infectious organism. The second is you have the attenuated organism, in this vaccine preparation organism is treated with a chemical to destroy its ability to cause disease. One of the classical example is the polio virus.

So, the polio vaccine, the polio drops what we take in for the polio vaccination is nothing but the attenuated virus which this attenuated virus means, it will not be it will still be able to propagate but it will not be able to cause the disease. As a result, organisms grow and gives stimulation to the immune system for a long term immunological memory. So, once if you give the polio drops to the baby it actually allowing this particular virus to replicate in to its gut. It allows the particular virus to remain in the system for very long time.

But, because this virus is attenuated it cannot cause the disease, the baby is keep generating the antibodies, keep generating the other kind of immune responses against these viruses. And, as a result at the end it is actually causing, the very robust immune response. It actually causes a large production memory B cells. And that is how the baby is going to have very long term protection against the disease. Then you have the toxoid in this vaccine preparation, inactivated toxic compound are used as an immunogen to train the immune system.

Then you have the subunit vaccine in this vaccine preparation, a pure protein or antigen is given as an immunogen, it is safest form of vaccine with minimal side effects. One of the classical example of subunit vaccine is the hepatitis vaccine. The vaccine is what you use for hepatitis is actually the hepatitis surface antigen. What you have cloned during the using the recombinant DNA technology. And, then you produced the protein like the surface antigen and this surface antigen you are injecting in to the human beings.

So, that the body is developing the antibodies against that surface antigen. And, that is how you are actually developing the robust immune response against the hepatitis virus. Then you have the conjugate vaccine in this vaccine preparation, the bacterial coat is tagged with the immunogenic protein to induce production of immune response against the bacterial coats. If, you would like to be interested to know more about the vaccine this different types of vaccines or how the vaccination is being done, you can follow any immunology text books such as you can follow the Roitt's Immunology or you can use the Genes Kubis Immunology and any standard immunology book can be refer for this purpose. If you would like to be interested to study more about the vaccinations.

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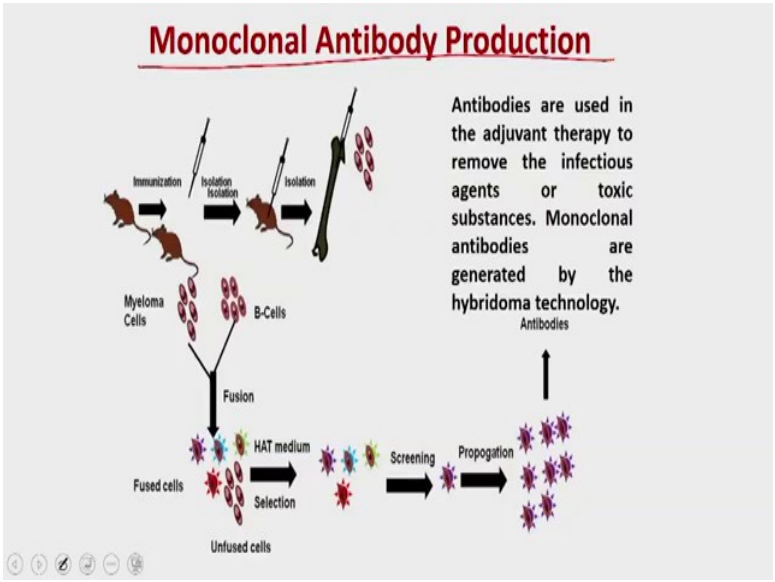

Before we go into the monoclonal antibody productions, what we have discussed so far. We have discussed about the applications of the biotechnology in the medical sciences. We have discussed about how biotechnology has allowed this production of the different types of vaccines. How it has allowed the production of different types of therapeutically relevant recombinant proteins. And, how we are, we with the help of the biotechnology we are actually performing the gene therapy applications. So, with this I would like to conclude our lecture here, in our subsequent lecture we are going to discuss about the production of monoclonal antibodies as well as the some more application of biotechnology in the other field as well. So, with this we would like to conclude our lecture here, thank you.