Legal and Regulatory Issues in Biotechnology
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Module – 02
Intellectual property Rights and Biotech inventions
Lecture – 08
Patenting issues in biotechnology (continued)

So, welcome back. We were discussing regarding the Patentability issues in biotechnology; continuing that.

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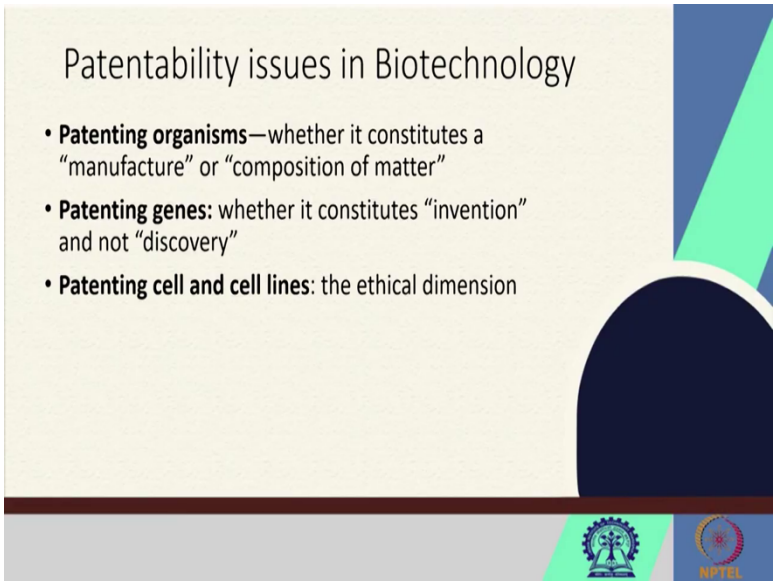

So, now the patenting challenges with respect to patenting the organism or the genes or the cell or the cell lines basically remains in deciding whether or not that article would be considered as an invention under the purview of the patent Act or it is mere discovery and if it is an invention, whether it is like meeting the other criteria or not.

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In general patent law across the countries do not allow discovery to be patented. So, discovery is something which is already present in the earth and you are just taking it out. And an invention is that where with the help of the human endeavor you are imparting a certain new form or new quality or at least some new properties to the original product which is existing in the nature.

So, the human interventions make the discovery into a patentable subject matter. You cannot claim mere the originally existing microorganisms or those microorganisms that are present in the earth crust or in the sea or the ocean beds, and, the isolation of those microorganism are also not a patentable subject matter

You can claim isolation methods where you have tried certain new techniques to isolate those things from the nature that may be patent eligible provided that meets the different criteria. But when it is about the microorganism which is already known or which is already existed in the earth, cannot be considered for a patentable subject matter.

And the controversy regarding that whether or what kind of microorganism is patentable or not patentable, was solved. It was decided through a landmark case which is known as the Diamond versus Chakrabarty case of 1980. And after this case it became clarified that modified microorganisms can be patent eligible or can be patented and that had prompted the formations of many companies where they have started developing the bio engineered products.

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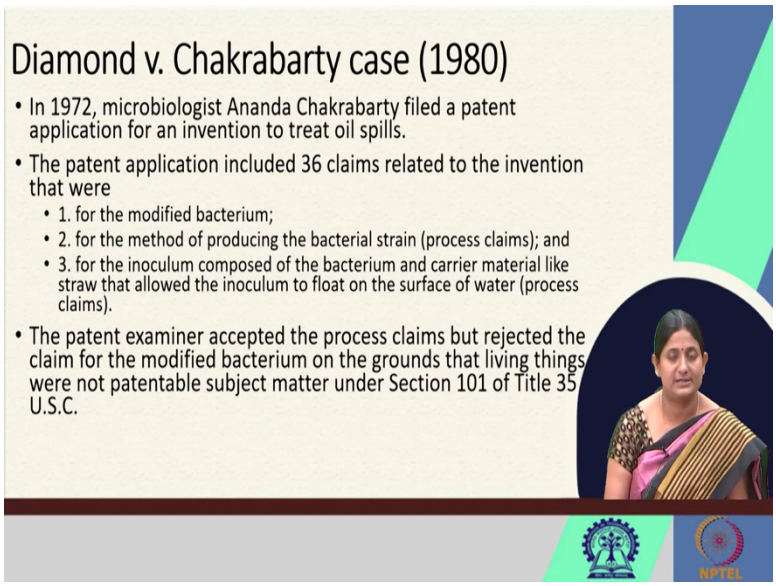

To just give you briefly the facts about this Diamond versus Chakrabarty case. So, basically micro biologist Professor Ananda Chakrabarty, filed a patent application related to an invention for the treatment of the oil spills in the year 1972.

So, what he did was that he isolated certain strains of the pseudomonas bacterium, which has the capability to degrade the fatty acids or hydrocarbon compounds that they use as an energy source and he tried to form a mixture of the different types of the pseudomonas strains which has the ability to degrade various types of hydrocarbons and with that mixture he tried to treat the oil spill.

So, if when he made a consortium with that, with different strains of the microorganism of the pseudomonas that was not effective. So, he then understood that the plasmids carried certain genes which is responsible for the degradation of the hydrocarbons.

And then he tried to make a new strain where he basically put all those as hydrocarbon degrading genes together and made a new strain of pseudomonas which has a high efficiency in degrading that hydrocarbon or the oil spill.

So, that patent included 36 claims related to the modified bacterium where different hydro carbon degrading genes in terms of plasmid were incorporated. The method of producing the bacterial strain which is basically your process claim and the inoculum

which compose the bacterium and the carrier material like the straws which allowed the inoculum to float on the surface of the water again which was a process claim.

So, the patent examiner only approved the process claim, but he rejected the modified bacterium on the grounds that no living organisms cannot be patented under the Section 101 of the US patent act or 35 U.S.C. And this was further challenged. So, Dr Chakrabarty challenge this verdict of the patent examiner.

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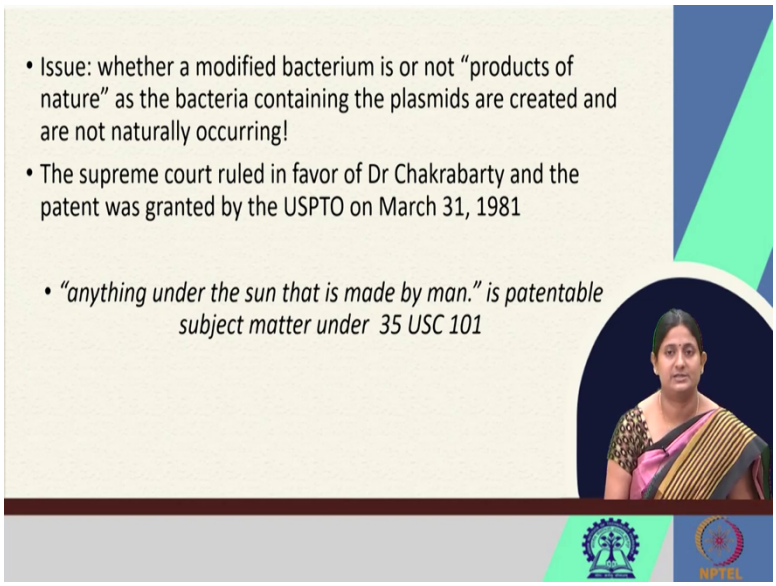

And then it was a long battle and it went to the Supreme Court and so the major issue was whether a modified bacterium would constitute an article or an subject method for the patent or not. So, the modified bacterium whether or not it is a product of nature so; however, the Supreme Court ruled in favor of Dr Chakrabarty and finally, the patent was granted by the United States Patent Office on 31st of March 1981. And there the bench and the jury they cited- anything under this sun that is made by man is patentable.

So, that became very popular that does not mean anything it was related to the bacterium strain. Basically what the jury considered is that even though the pseudomonas strains were isolated or they were present differently in the nature. But the strain which Dr Chakrabarty created was not originally present it has been created. A person did not included the core biotechnology or the recombinant DNA part, but still by human interventions he had tried to made make a modified bacterium.

So, modified bacterium can be a patent eligible subject matter under this Section 101 of 35 USC 101. So, this was the landmark case after which lot of companies have started patenting different modified strains of the bacteria or the microorganisms and try to develop new process. So, this is one of the very important decisions in the history of the United States that has favored the biotech industry.

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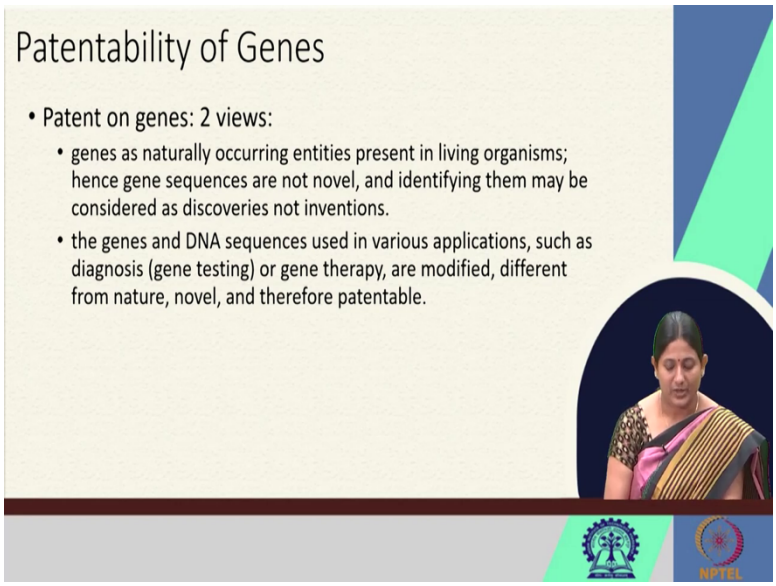

Similarly, when we talk about the patentability of the genes - we have again two views there, because you know our the human cells or any animal cell is composed of certain nucleic nuclear material. So, the nuclear material may be in the form of the DNA or the RNA and each of this DNA has certain character which they express. So, these are the basic units of the life which is known as the again genes.

So, the genes are present naturally in the living organism. Those who oppose this view, that the gene should be patented, they oppose it because of the fact that gene sequences are already present therefore it is not a new. So, you have just identified the genes, which is already present in the body of certain living organism.

So, that may not come under the purview of an invention. You may say it is a discovery where you have isolated or you are just taking out or telling that sequence of the gene, but there is no change in that gene. So, it should not come under the purview of the invention.

The second group they propose that the genes or the DNA sequences are useful in the various application. For example, the diagnosis where you can check for various genetic diseases or it may be useful for the gene therapy. So, when the isolated gene are used for various purposes and meeting the industrial applicability requirement so, it should be patentable.

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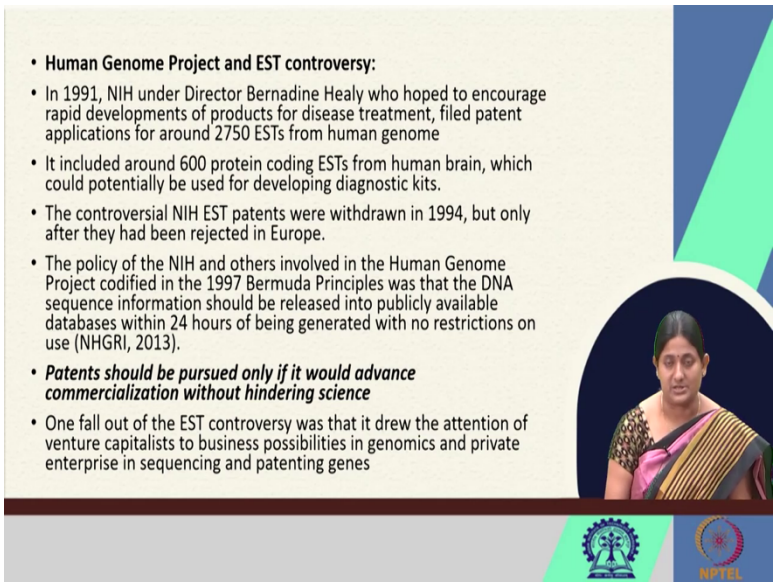

So, again there is lot of controversies regarding this. Now, if we again go back to little bit of history we will find that when the human genome project has started and scientists started decoding the human genes, lot of information were available. So, in the year 1991, the then NIH National Institute of Health director Bernadine Healy thought that with these kind of discoveries or the invention where the human genes has been decoded, we can develop number of products which will be helpful for disease treatment and that is why he filed around 2750 expression sequence tags from the human genome and it also included around 600 protein coding ESTs from the human brain, which would be potentially useful for developing diagnostic kits.

And they have applied patents in Europe, America as well as in Australia and Italy. So, the application was filed in many countries; however, it drew a lot of controversy. So, finally, in the year 1994 the NIHEST's patents were withdrawn, one reason was that the patent was not granted in Europe, as the criteria of patentability is quite strict compare to the United States of America.

So, the question was the next director of the NIH they have consulted with the US patent office to understand whether or not the patents in this area should be pursued. So, their advice was that the patent should be pursued only if it would advance the commercialization and it should not hinder the scientific development. But by patenting this expression sequence tag it may raise the competition among the private players and it would be basically because patent is a monopoly right.

So, it may hinder the development of the science rather than promoting the commercialization. So, for that reason they withdrew the patents, but; however, once this process has started and where number of venture capitalist started exploring business possibility in the area of the genomics and the many private enterprises entered into the sequencing of the genes or the nucleotide product.

So, this was the first time when the use usefulness of the genes or the ESTs were seen or had applied as a patentable substance.

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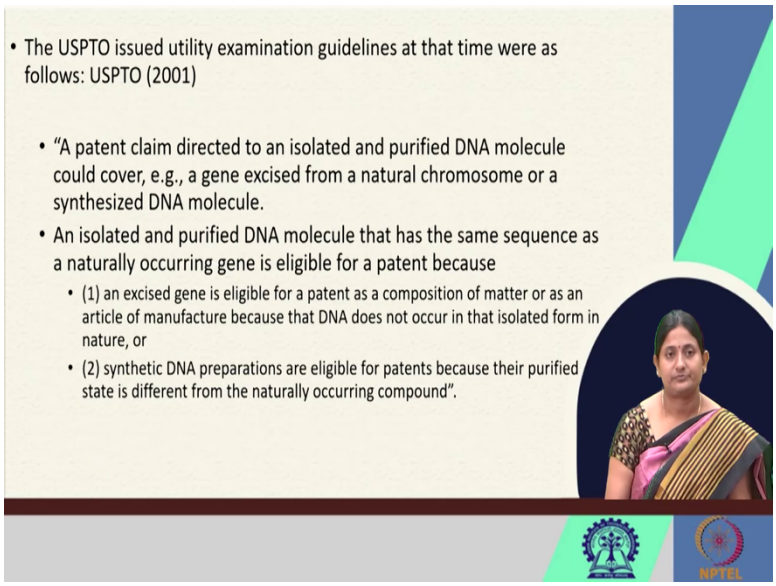

And finally, at the time in 2001 the United States Patent Office, had also given certain examination guidelines about what if a patent has been applied for a gene related product then what can be considered as a patent eligible and what may be rejected.

So, if a patent claim directed to an isolated or the purified DNA molecule, it may cover the gene excise from the natural chromosome or a synthesized DNA molecule. And so in

this case the isolated DNA molecules were allowed as a patentable because it is isolated and so it was not found in the isolated form.

So, if someone is isolating a gene means the human intervention is made then that is the reason it was allowed as a patent at that point of the time. And further if the isolated and the purified DNA molecule has the same sequence as the natural occurring gene it may make them patent eligible. Because it acts like a composition of the matter and as it is not naturally occurring in that form.

And if it is a synthetic DNA, it may be patent eligible because again it is not available in the purified form and it is different from the naturally occurring compounds.

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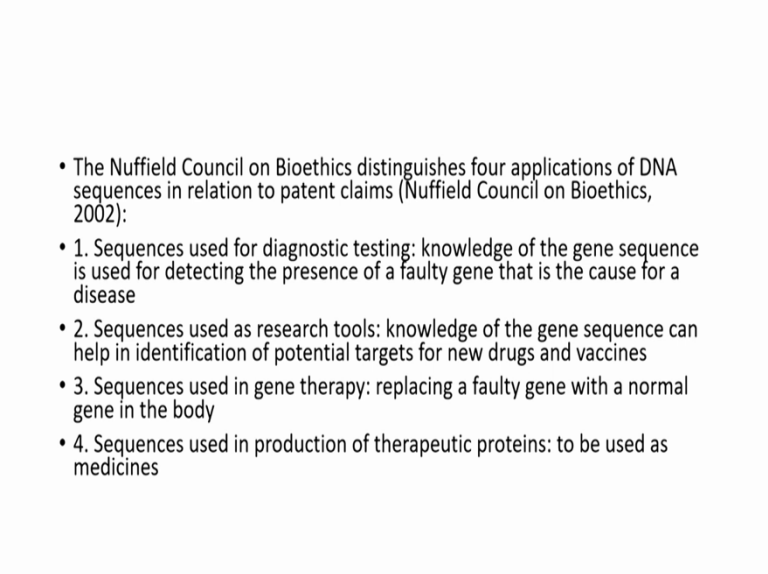

And further the Nuffield Council of the bioethics distinguished different application of the DNA sequences which can be related to the patent claims. For example there may be sequences which are used for the diagnostic testing and there may be sequences which are used for the research tools. Like if there are genes sequence which can be helpful in the identification of the potential targets for the new drugs and the vaccines, that is useful,can also be patented.

Sequences sometimes may be used in the gene therapy, where a faulty gene is removed and in place a normal gene is inserted and then there are different sequences which are used in the production of the therapeutic proteins which are used as the medicine.

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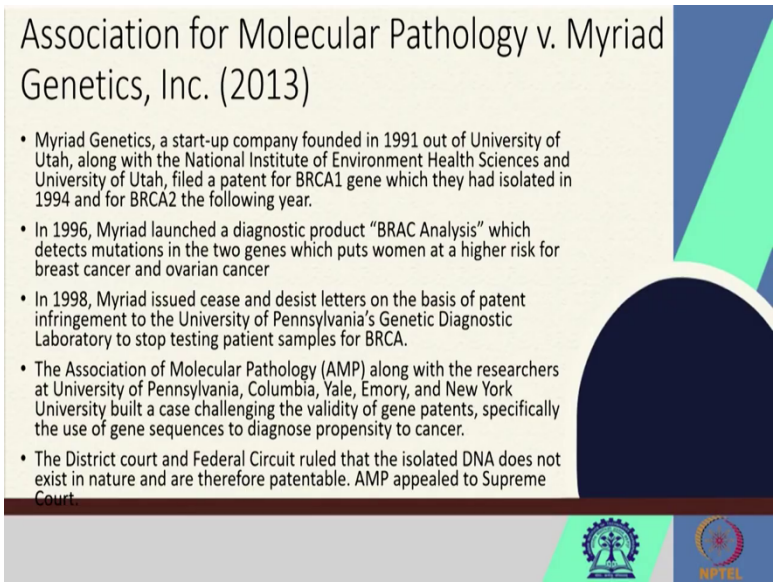

So, depending on the use of the substances there are some cases where patent on the genes are allowed and there is another landmark case of Association of Molecular Pathology versus Myriad Genetics in 2013 which has again changed the landscape with respect to the gene sequence.

So, again, just to give you facts of the case, the Myriad Genetics is a start-up company founded in 1991 out of the University of the Utah. So, they along with the National Institute of Environmental Health Sciences of University Utah; filed a patent for BRCA 1 gene or the BRCA gene which is popularly known BRCA 1 and BRCA 2.

So, basically these genes are the genes which were helpful in identifying whether a woman can develop breast cancer or not. So, in 1996 the Myriad Genetics launched a diagnostic product known as the "BRAC Analysis" which is basically a thing that detected mutation in these two genes BRCA and BRCA 2 and it identified like which women is at a higher risk of developing the cancer, breast cancer and the ovarian cancer.

So, once this technique was out lot of other companies also started using the technology without the permission of the Myriad Genetics. So, since Myriad has the patent on the BRCA 1 and BRCA 2. So, they have the monopoly on that and no one is suppose to use those things, but other company started using that.

So, as a preventing measure in 1998 Myriad issued cease and desist letters on the basis, citing it as a kind of patent infringement activity which the other companies were doing. So, they sent notices to different companies or the University of Pennsylvania to stop these testing of the patients' sample using this BRCA.

But again since this was a naturally occurring gene BRCA gene, so the Association of Molecular Pathology along with the researchers of the University of Pennsylvania, Colombia, Yale, Emory and the New York University built a case challenging the validity of such kind of the patent.

And specifically the use of the genes sequence to diagnose the propensity of the cancer. So, initially the district court as well as the federal circuit court held that the isolated DNA does not exist in nature and there should be patentable. But to this decision the association of molecular pathology they appeal to the Supreme Court.

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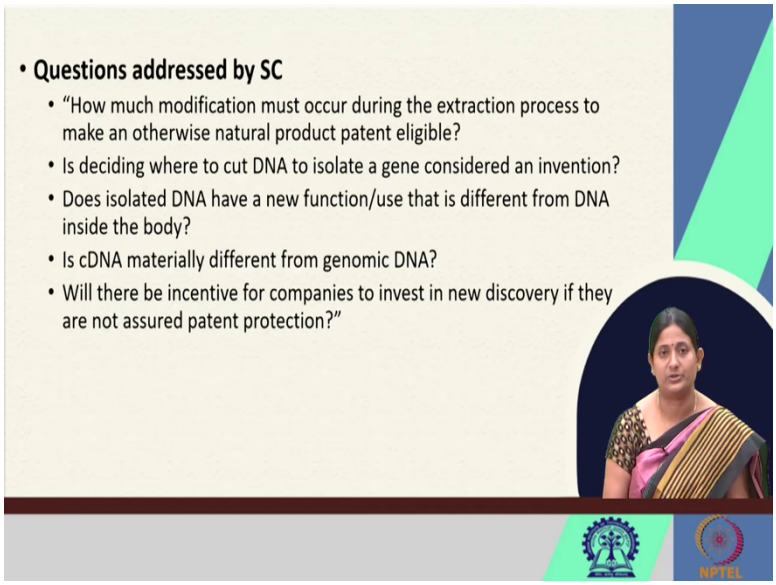

And in the Supreme Court the court basically looked into, how much modification would we be looking into a gene product or into the extracted product that would make a gene as a patent eligible subject matter? And what are the factors we should take into account while we consider that discard DNA or the isolated gene DNA is considered as an invention? Will it be the new function or how different is the DNA from the inside, the DNA which is existing outside and which is there in the body?

So, how we can compare the complimentary DNA with a genetic DNA? And if we stop this kind of the patenting then, what incentive would remain for the companies to go for new discoveries,

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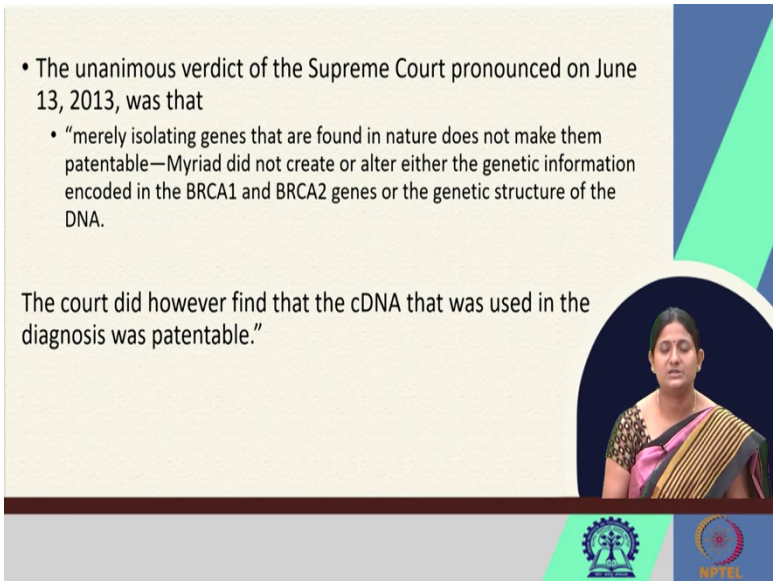

If they are not assured of patent protection? These were the few questions they considered and finally, the verdict of the Supreme Court was that merely isolating genes that are found in nature, are not patentable. So, the Myriad did not create or alter the genetic information encoded in the BRCA and BRCA 2 genes and the genetic structure of the DNA. So, the isolated BRCA 1, BRCA should not be given patent.

However, the complimentary DNA which is again a changed version of the DNA was not something which occurred naturally and again it is useful for the diagnostic purpose. So, that complementary DNA is patentable, but not the BRCA and BRCA. So, after this decision in 2013 mere isolation of the gene was again not held patentable.

So, it has changed the whole landscape of the gene patenting provisions in the United States. And also in the Australia later on there are cases which also in the same way did not allow the mere isolation of the genetic sequence from the human genes. Only and if the genetic sequences altered or it had sufficient function to attach to it may be diagnosis, it may be treatment or development of any therapeutic purpose then only it was held patentable.

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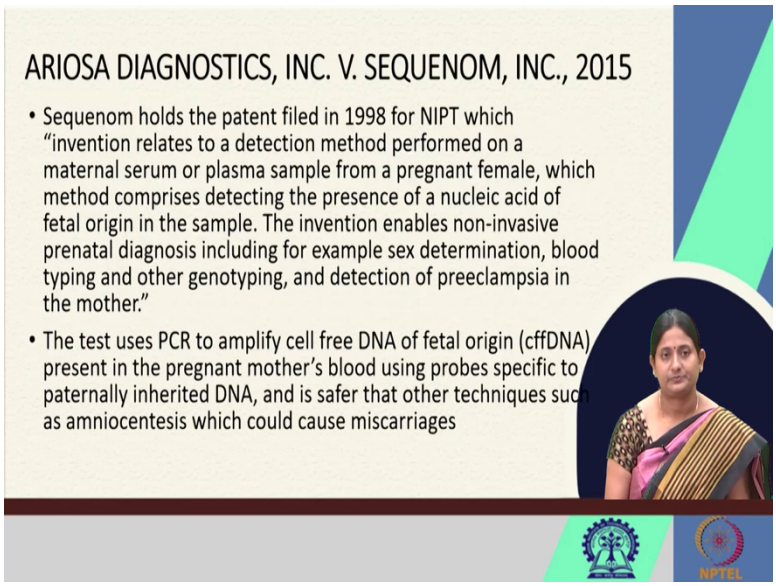

And similarly, there is another case Ariosa Diagnostic versus Sequenom in 2015 where this Sequenom Company held the patent for this NIPT which is basically a method for detection of the down syndrome and it included a provision where the plasma sample from a pregnant female was taken were collected and then the presence of the nucleic acid of the fetal origin was tested with respect to the paternal DNA.

So, this method had many advantages with respect to the earlier available method which was more invasive and which may cost miscarriages. So, the patent was given to the Sequenom.

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Again so, after this Sequenom launch this diagnostic method in the market, number of other companies started using the same and then this Sequenom filed patent infringement against those companies. So, the other companies again, challenged the patent.

So, the district court in this case held that the claims are patent ineligible on the grounds that, "the claims at the issue pose a substantial risk of pre-empting the natural phenomena of paternally inherited fetal DNA" and it again. So, this Sequenom Company appeal to the Federal Circuit.

But; however, the Federal Circuit again affirmed the judgment of the district court and held that the claims which the Sequenom had are "directed to the patent ineligible concept" as the claimed method did not transfer the claimed naturally occurring phenomena into patent eligible because that paternal DNA is existing in there. So, by just taking that concept and developing a diagnostic kit would not be a provision and you cannot debar others from using that technology.

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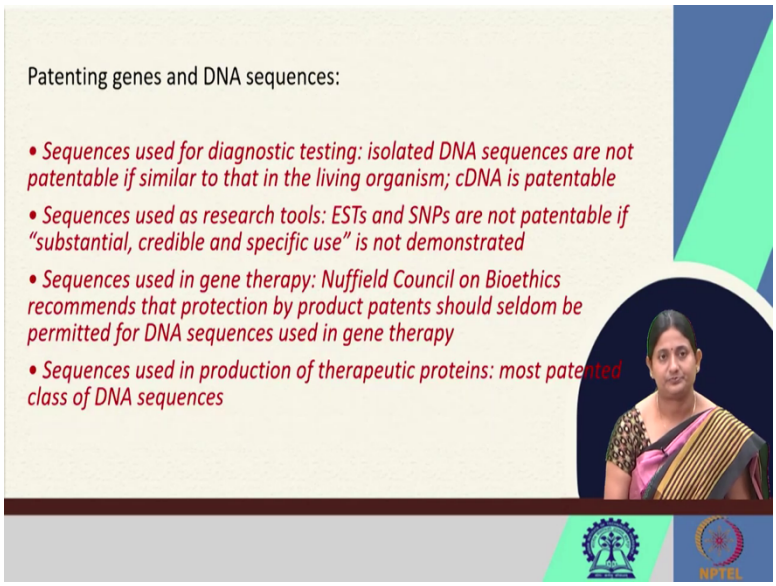

So, these are the cases which has led a change in the total outlook in which the patenting of the genes has been looked in the United States. So, finally, when we see the current provisions the patenting of the genes and the DNA sequences is allowed if again the if the DNA sequences are not similar to the living organism and or those complimentary DNA is patentable.

Sequences which can be used as a research tools say for example, the expression sequence tag or SNPs are not patentable if the utility is not substantial. So, you have to show substantial credible and specific utility to show that the thing or the sequences are useful.

And sequences used in the gene therapy actually is rarely permitted because you know if a gene is faulty the definite way out is to replace it with the natural occurring gene or the good gene. So, it should not be given patent and yes sequences used in the production of the therapeutic proteins are mostly patented and it is very much helpful for the development of the new therapeutics as well as it acts as an incentive for the companies. So, this is with respect to the gene patenting.

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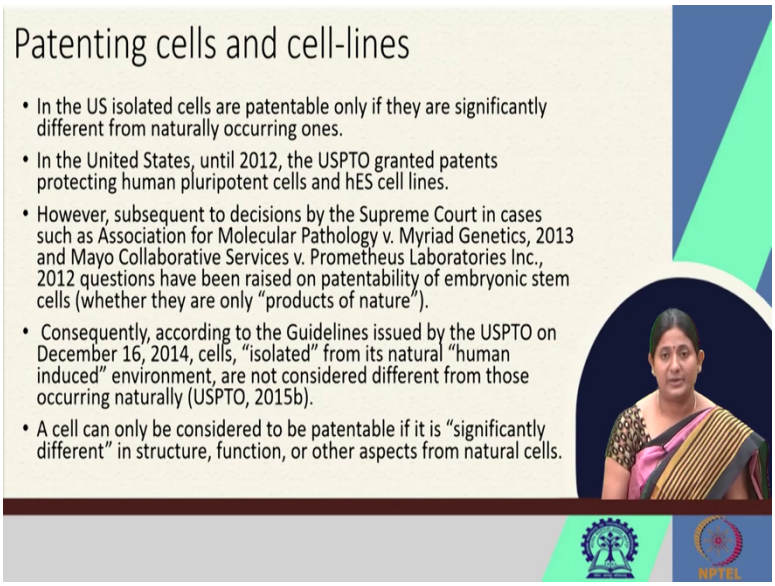

The third issues with respect to the patenting of the cells and the cell lines is that in United States the isolated cells were patentable only if they were significantly different from the naturally occurring genes. So, as we saw till 2013 and when the Myriad decisions were not given, the USPTO granted patents with respect to the human pluripotent cells as well as the human embryonic stem cell lines.

However, after the subsequent decision by the Supreme Court it has changed and in 2014 the USPTO further issued certain guidelines. So, "isolated" from the natural "human induced" environments were not considered as naturally occurring. And a cell can be considered to be patentable if it is "significantly different" in the structure, functions and other aspect of the natural cells.

So, those were the recent changes after 2014 to the human embryonic stem cell research in the United States. Unless and until it is substantially different -it is is not patentable there.

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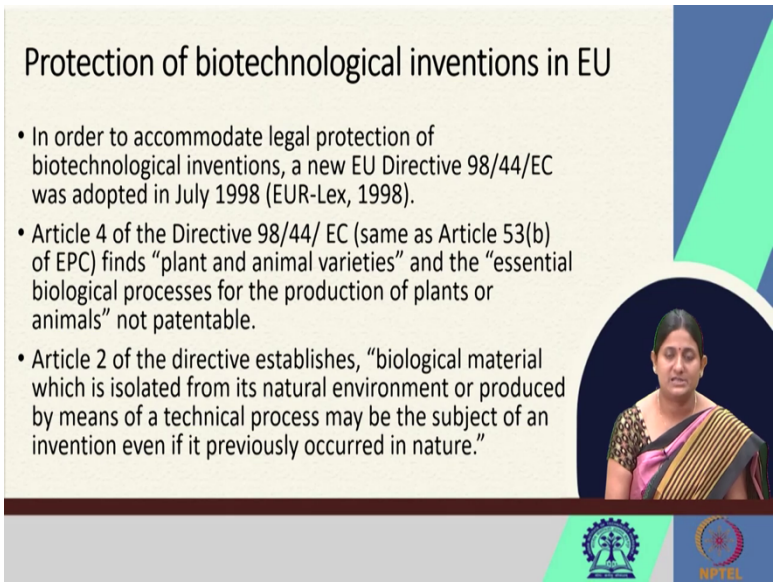

So far we have discussed about the United States, but if we come little bit to the European Union. In Europe the things are taken little bit differently. So, the public order morality concept or particularly patent with respect to biotechnological invention is considered as a serious matter there.

So, they have a particular directive which is known as the biotechnology directive 98/44 EC which was adopted in the year 1998. So, the directive gives a lot of guidelines what aspect of the biotechnology could be patented. For example, the Article 4 of the Directive finds that the "plants and the animal varieties" and other "essential biological processes for the production of the plants and animals" are not patentable.

And Article 2 of the directive establishes that the, "biological material which is isolated from the natural environment are produced by means of the technical process may be the subject of invention even though it is previously occurring in nature."

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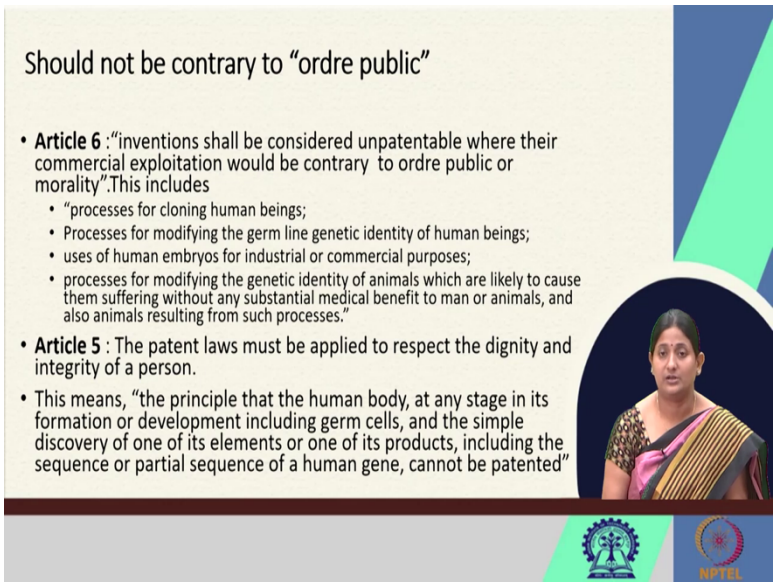

But the important issue to be considered is that the invention should not be contrary to the public order or the morality. For example, in the human embryonic stem cell research or the process of cloning of human beings or process of modifying the germ line in the modify the germ lines which basically changes the genetic identity of the human beings; huge use of human embryos for the commercial purposes, and the process for modifying the genetic identity of the animals which may cause them suffering without any substantial medical benefit to the man or the animals and animals resulting from those process were not patentable because it is something which is considered as against the public order.

So, the main important provision which the EU directive relives is that the patent laws must be applied to respect the dignity and integrity of a person. So, if you are destroying a human embryo; that means that you are destroying the human dignity because they consider the human embryo to be equivalent as a living organism.

So, the principle is that the human body at any stage in its formation or development, including the germ cells or the discovery of any element of the cells or the partial sequence of the genes cannot be patented there. So, here in Europe compared to the US, they adopt a stricter guideline or stricter provision in patenting the human cells or human genes.

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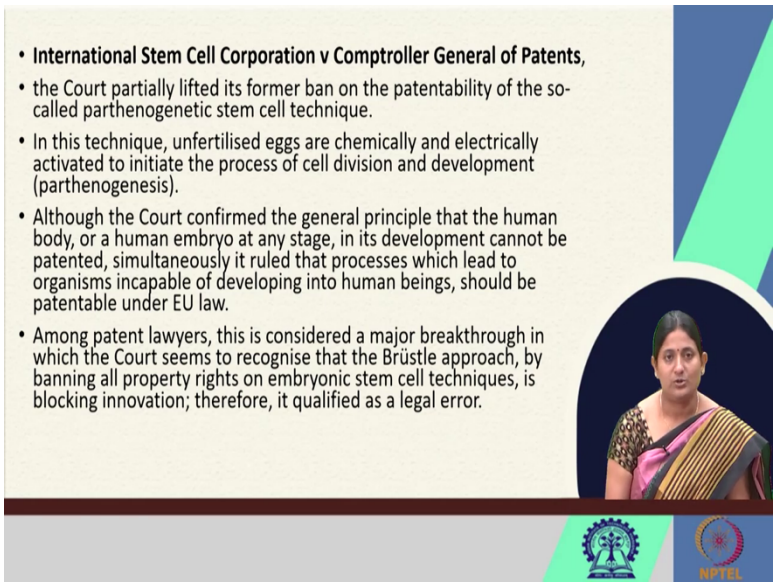

So, recently there have been certain changes to this aspect. In the International Stem Cell Corporation versus the Comptroller General of the Patents, is a case in the European Court of justice, the court lifted the formal ban on the patentability of the parthenogenetic stem cell technique. So, any intervention on the human embryonic stem cell is strictly forbidden because it considers the human embryo to be a living organism.

But when the stem cells were developed from the parthenogenesis process that is the human induced pluripotent stem cells or human parthenogenetic embryonic stem cell that is somatic cell. It is confirm somatic cell that is transferred into pluripotent cells or the process of parthenogenesis cell has been changed. Hence, this gave a little bit relaxation to the earlier strict criteria.

Although the court confirm that the human body or the embryo at any stage of the development cannot be patented it gave a little bit provision that organisms incapable of developing into the human beings should be patentable under the European law. So, it is now considered as a little bit of relaxation or break through which the court has given in the earlier, Brustle case, this case banned all the intellectual property rights of the embryonic stem cell techniques, means no inventions related to the embryonic stem cell development or associated techniques would be patentable.

However, after this case it gave a relaxation that ok human embryonic stem cell cannot be patented, but the associated techniques can be allowed to be patented.

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So, like in the Brustle case in 2011 that basically excluded all the human embryonic stem cells and the patentability of the other techniques if it results in 'the prior destruction of the embryo or they are used as a based material, whatever the stage at which it takes place'.

So, no process in around the embryonic stem cells were allowed and, but there were again debate over how do you define the embryo, like at what stage you are saying that the human embryo is equivalent to the living organism. Whether the concept of totipotency is considered as a factor or not ;or whether we consider a pluripotency stem cells as same as a totipotent stem cell.

So, thereby there are debates. Anyways, the crux of the matter is that the human embryonic interventions or human embryonic stem cells, as such is not patentable. But yes, associated technique which may result in other developments may be allowed as a patentable subject matter.

So, this is the controversy regarding the cell and the cell lines across US and EU and India as we said. So, in India also we do not allow patent on the human embryonic stem cells. The isolated gene sequence are patentable but only if it has changed its substantial utilities. These are observed in case of the India as well. So, this is for this lecture. We will discuss more about the other issues in the upcoming lectures.

Thank you so much.