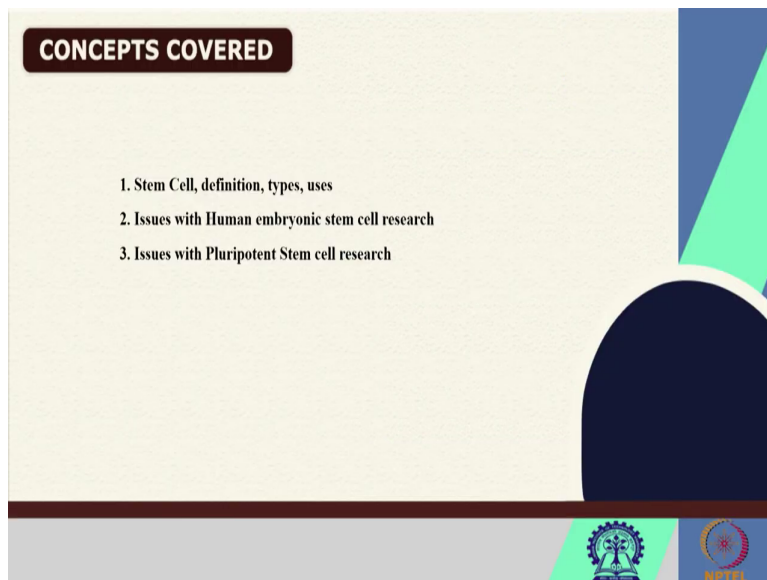


Legal and Regulatory Issues in Biotechnology
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Module - 01
Regulation of Biotechnology Research
Lecture - 05
Ethics in Stem Cell Research

Hello all, welcome back to the sessions in the 1st module. So, we in the earlier classes discussed regarding the clinical trial or ethics in the clinical trial of the biotechnological product. So, in today's lecture we are going to deal in deal with one of the majorly growing areas of the biotechnology that is the Stem Cell Research.

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So, in this lecture particularly we will be dealing with the aspects of the ethics and other issues with respect to stem cell research. And we will see how the research related to the human embryonic stem cells has become a concern in the area of the current biotechnological research and what are the other ways it has been overcome and also the associated issues with that too.

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Regenerative Medicine and Stem Cell

- “Regenerative medicine” describes a set of innovative approaches to the treatment of illness, injury, and disability, focusing on the growth, replacement, and repair of cells, organs, and tissues specific to the health needs of particular individuals.
- Progress is clear from an enumeration of just a few of the areas of regenerative medicine research:
 - stem cells, including
 - pluripotent embryonic stem cells,
 - pluripotent stem cells produced by genetic reprogramming, and
 - multipotent stem cells from fetal, perinatal, pediatric, and adult tissue



So, the stem cells are the kind of the cells which has the ability into which has the ability to differentiate into different kinds of the cell. So, human body is like we have different types of the stem cells depending on from which cell the stem cells has been derived which can regenerate into different tissues or different cells depending on its site or depending on the place where it is situated.

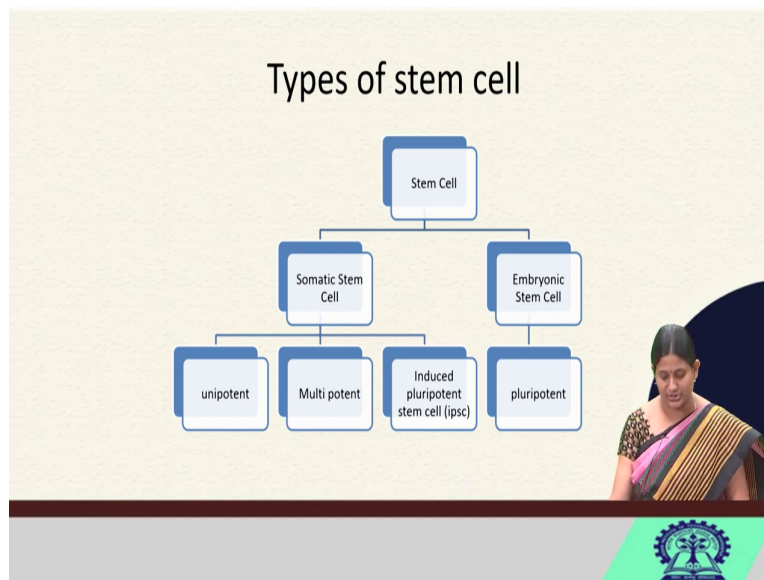
So, this ability of the stem cells where it can regenerate into different tissues has been exploited in the biomedical sciences and that has given to the domain of the regenerative medicine or stem cell tissue therapy. So, this regenerative medicine is basically described as a set of innovative approaches which is used for the treatment of the illness or the injury and which basically focuses on the growth, replacement and the repair of the cells or the organs or specific tissues depending on the health need of the particular individuals.

For example, it may be in the case of the diabetes where you need to replace the pancreatic tissue or it may be in the case of the brain disorder like Parkinson's disease where the nerve cells may need to be replaced. So, in these areas where we do not have specific treatment. The regenerative tissue approach or the stem cells can act as a miraculous thing.

So, in the broad area of the regenerative medicine we have different area of research like the stem cell research. And the stem cell research not only includes the somatic stem cells it also

includes the embryonic stem cells like the cells which are derived from the embryo. And there are they are also categorized into different types like depending on where they are used and how they are used, so, and the ability of the tissue to differentiate into what kind of the cells. So, it may be multipotent stem cells or it may be pluripotent stem cells.

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For example, so, depending on the place from where these cells has been developed like it may be a somatic cell stem cell or it may be embryonic stem cells when particularly it is derived from an human embryo or the fetus and again depending on the ability to regenerate. So, when a stem cells give rise to a particular type of tissue or the cell it is unipotent then there are multipotent stem cells, where it may differentiated into related categories of the cells.

And there is another category is called induced pluripotent stem cells, where the somatic stem cells are induced to become and to behave like a pluripotent stem cells, which is the stem cell which can regenerate into different types of the tissue. It means all the tissue types which is available in the human body. So, this is basically I just to give you a brief introduction to this area.

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Issues in stem cell research

- **Ethical consideration**
- Arguments about human embryonic stem cell research;
- safety concerns raised by induced pluripotent stem cell research;
- the ethics of research design;
- issues to consider the first time an intervention is tested in human subjects; and
- informed consent and the therapeutic misconception



Now, coming to the issues with respect to the stem cells research, so, what kind of problem do we face? And as we have been discussing in case of the biotechnological research the ethical considerations becomes first and foremost major issue while we deal with the biomedical research. For example, here when we are talking about an embryonic stem cells.

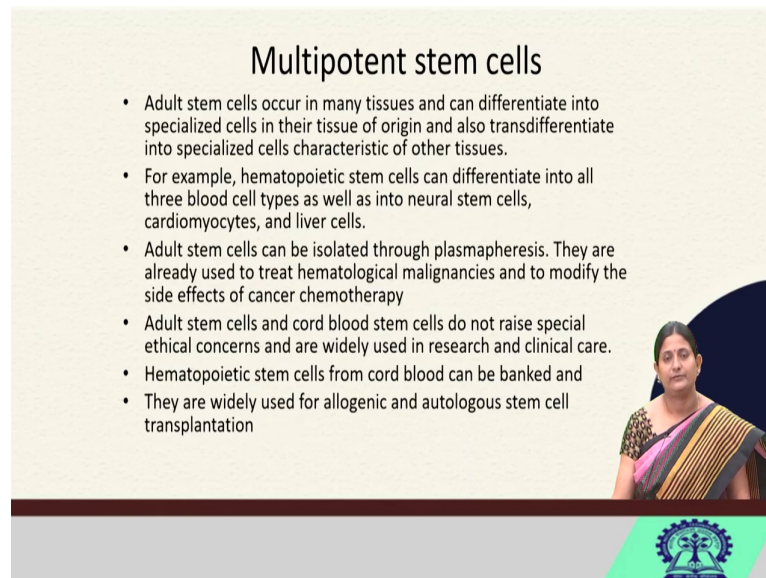
So, then arguments related to the status of the embryonic stem cells, is it really ethical to use an embryo for research purpose? That becomes a question. Then also there are certain safety concerns raised by the induced pluripotent stem cells, where the with the with various genetic interventions the somatic stem cells are converted into induced stem cells with multi pluripotent activity.

So, again it is easier to say, but in practical when it is done there are a number of issues or health concerns or safety concerns which has been observed. So, that is one of the major considerations also. And how the research is designed particularly in the case of this biomedical thing and in the stem cell is another important area. The number of embryos used or the how the other specimens have been used in this whole process that becomes issue here.

Then, the issues to consider the first time and intervention when it is tested in the human subjects and also the problems related to the informed consent and therapeutic misconception. So, these are the major issues which generally which are generally faced

during the stem cell research. So, in the next few slides, I would be dealing one by one with these areas.

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Multipotent stem cells

- Adult stem cells occur in many tissues and can differentiate into specialized cells in their tissue of origin and also transdifferentiate into specialized cells characteristic of other tissues.
- For example, hematopoietic stem cells can differentiate into all three blood cell types as well as into neural stem cells, cardiomyocytes, and liver cells.
- Adult stem cells can be isolated through plasmapheresis. They are already used to treat hematological malignancies and to modify the side effects of cancer chemotherapy
- Adult stem cells and cord blood stem cells do not raise special ethical concerns and are widely used in research and clinical care.
- Hematopoietic stem cells from cord blood can be banked and
- They are widely used for allogenic and autologous stem cell transplantation



So, before coming into adult or the embryonic stem cells let us first discuss about the multipotent stem cells. So, the multipotent stem cells are basically derived from the adult stem cells which are present in various tissues and they have a kind of ability to differentiate into specialized cells and basically they gradually trans differentiate into various specialized cells which have particular characteristics and other tissues.

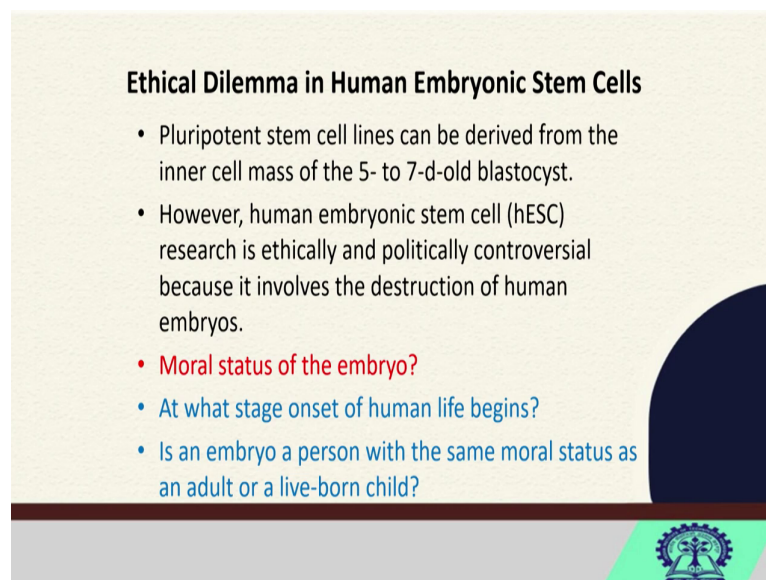
For examples, these hematopoietic stem cells, the blood stem cells if you can if generally said. So, they have the ability to differentiate into the three blood cells type like the RBC, WBC or platelets and also, they may differentiate into the neural stem cells or the cardiomyocytes means, the cells present in our heart which develops into the heart or the liver cells.

So, these are the specialized cells have a limited ability to differentiate related group of the tissues. And these stem cells are separated from the adult stem cells through a process known as the plasmapheresis. And these are already been clinically well proven and has been in use and basically these multipotent stem cells has been have been used in the treatment of the hematological malignancies.

And it also it is also majorly used for the treatments of the side effects arising out of the cancer chemotherapy. So, this is one of the areas where already much research has been done and it has been proved quite a safe procedure to carry out these things. And because these are derived from the somatic cells or other stem cells.

And generally used in the specific or homologous individual this adult stem cells are the cord blood stem cells do not raise special ethical issues. And it is been widely used in research and clinical trials across the countries including India. And basically, as I mentioned it has been widely used for the allogeneic as well as the autologous stem cell transplant. So, means, related individual or a from the in the same individual.

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Ethical Dilemma in Human Embryonic Stem Cells

- Pluripotent stem cell lines can be derived from the inner cell mass of the 5- to 7-d-old blastocyst.
- However, human embryonic stem cell (hESC) research is ethically and politically controversial because it involves the destruction of human embryos.
- **Moral status of the embryo?**
- **At what stage onset of human life begins?**
- **Is an embryo a person with the same moral status as an adult or a live-born child?**



However, when the research comes when the question comes to the area of embryonic stem cell research then the problem with related to ethics or ethical dilemma it comes into picture. Now, this pluripotent stem cells, means the cells which has the ability to differentiate into various types of the tissue.

So, that it can replace the damaged organs or it can replace the damaged tissues and can be an effective treatment method of very various diseases for which we do not have any effective treatment so far. So, but the problem is that these kind of pluripotent stem cells are generally

derived from the human embryo when the human embryo is around 5 to 7 days old, it divides into a mass of cells which are known as the blastocysts.

And these human embryonic stem cells are derived from these 5 to 7 days old blastocysts in their mass of the cells. But, this procedure makes it ethically as well as the politically controversial thing because it needs the destruction of the human embryo. So, once you take out the if you want to take out the human embryonic stem cells from the blastocysts we need you need to destroy that embryo.

So, there are different proponents or there are different arguments in or against the use of the human embryonic stem cells for in the biomedical research. One of the proponent like the main questions which is generally posed is that, what is the moral status of the embryo?

So, when you are going to destroy the embryo, so, are you really going to kill a living organism or it is just a mass of cells? So, can the embryo be equated with all full-fledged living organisms? If yes, let us begin the direct answer, but if no then when can we say that it is the perfect time that the human life has begun in that embryo and can we provide the same moral status as a live born child or as an adult to an embryo at that stage?

So, these are the few important questions which are generally raised and to be frank there is no settled principle. So, far it is a ongoing continuing argument among the proponent as well as the among the groups which oppose the research in the area of the embryonic stem cell.

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Ethical dilemmas with hESC

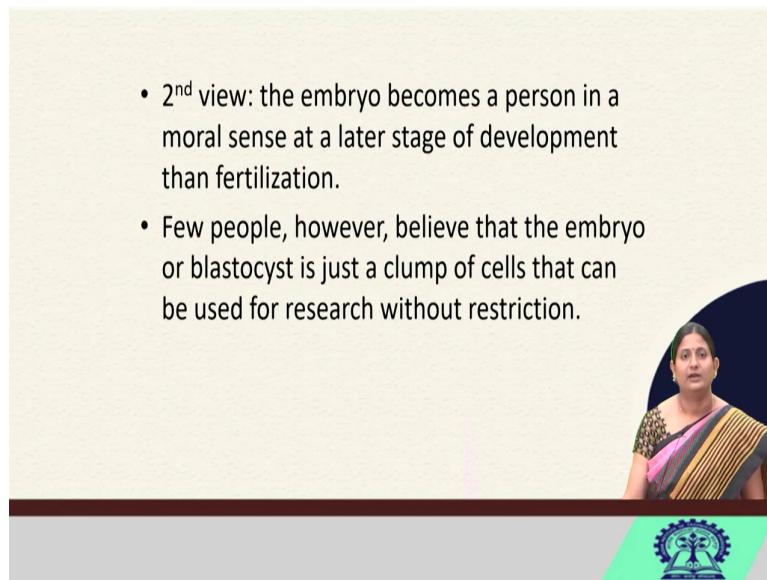
- 1st view:
- “Human life begins at conception”,
 - taking a blastocyst and removing the inner cell mass to derive an embryonic stem cell line is tantamount to murder



So, if you see majorly there are three views in the area of human embryonic stem cell research. As per the first group of people who believe or the pro-life category which of which we may say they believe that the human life begins at the conceptions. Means, when sperms meet an oocyte or develops into a fertilized egg and develops into a zygote from that stage itself the human life has started beginning.

So, if you are taking a blastocyst, and removing the inner cell mass to get an human embryonic stem cells then it is equivalent to murder of an full-fledged life live adult. So, they are very clear cut that ok You know were in inside the body of a human or a woman when the embryo or the blastocyst whether it is like 4 days or 7 days old from the very first day it attains the status of a full-fledged human being.

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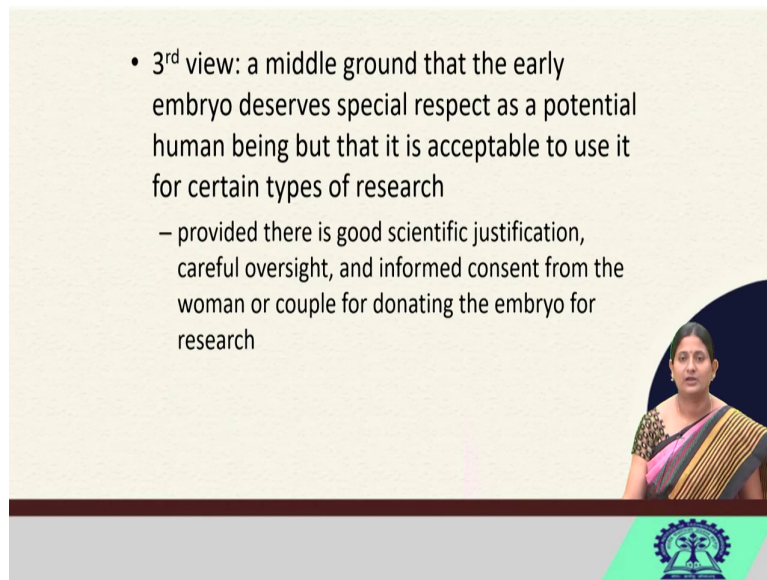


- 2nd view: the embryo becomes a person in a moral sense at a later stage of development than fertilization.
- Few people, however, believe that the embryo or blastocyst is just a clump of cells that can be used for research without restriction.

And then there are again 2nd view, which is little bit contrary to the first one. So, this belief that the embryo becomes a person in a moral sense at the later stage of the development than fertilization. So, we cannot really say or equate the embryo with a full-fledged individual. So, it is they believe that it is like a clump of cells. So, that needs to be further developed. So, that expresses the human characters.

Means, again there are few criteria means, some believe that till the time the primitive streak develops in the human that zygote or embryo then only we can consider them as a individual or at a live individual. Before that it is just a mass of cells and if you are deriving something some embryonic stem cells for the from them to carry out certain research then it should not be a problem.

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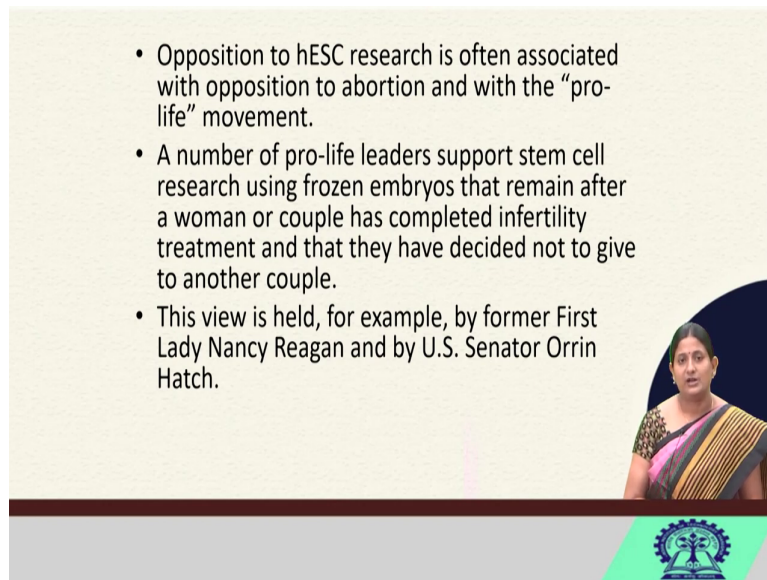
- 3rd view: a middle ground that the early embryo deserves special respect as a potential human being but that it is acceptable to use it for certain types of research
 - provided there is good scientific justification, careful oversight, and informed consent from the woman or couple for donating the embryo for research

Again, there is a 3rd view which is in which lies in between the first two views. They believe that the early embryo deserves special respect, but as a potential deserves the early embryo should deserve respect as a potential human being, but again when needed those can be used for particular type of the research.

Provided there should be a good scientific justification and it should be carefully evaluated again the pros and cons of social how much you what you are gaining out of the experiment and how much suffering you are giving by extracting those kinds of the cells that has to be properly weighted.

And proper informed consent from the woman or the couple who are donating the embryo for the research has to be, that they should get that thing and then this kind of research should begin. So, as I mentioned, so, this is an ongoing debate. So, whether or not to consider these 3 to 4 to 7 days old embryo as a full human being, so, that is continuous debate.

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- Opposition to hESC research is often associated with opposition to abortion and with the “pro-life” movement.
- A number of pro-life leaders support stem cell research using frozen embryos that remain after a woman or couple has completed infertility treatment and that they have decided not to give to another couple.
- This view is held, for example, by former First Lady Nancy Reagan and by U.S. Senator Orrin Hatch.

Because again as I mentioned, so, from the conception itself; so, they believe that the human life starts because there are certain emotional attachment or certain religious belief. So, we cannot really. So, this pro-life movement or the other person who believes in those things they believe that destruction of those kind of the embryo is not ethically justified.

And also it is related to the other issues of the abortion where deliberate abortion or abortions by which the through which they are getting the embryos and doing the other scientific research. So, that may expedite those process and it has been also a debate in the many western countries. And the number of pro-life supporters of this support this number of pro-life leaders support the stem cell research using the frozen embryo.

So, one of the way through which this issues of destroying the human embryo directly may be circumvented by the use of the frozen embryos. So, like in case of this IVF or alternative reproduction therapies, so, where the there are in vitro fertilizations or there are clinic reproductive clinics where these sperms or the eggs are fertilized outside the human body and majority of them are not used.

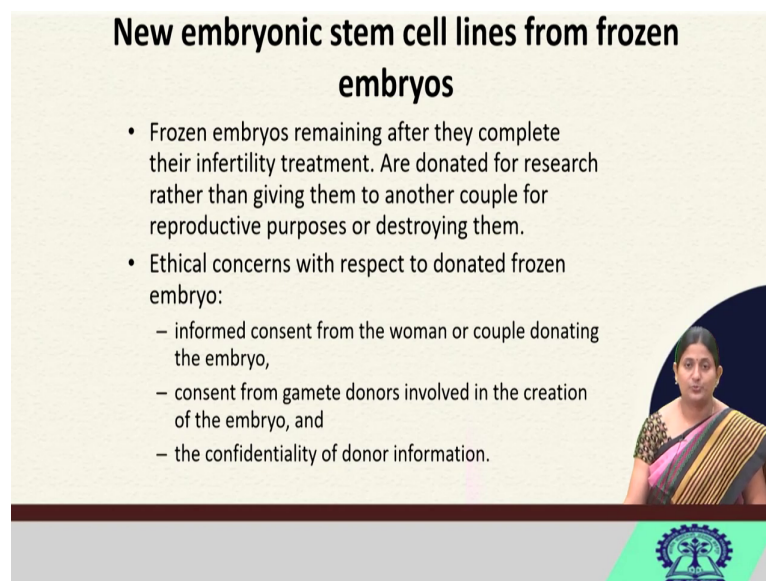
So, in those kinds of the zygotes if they are available or embryos which if they are they are available those can be used for this kind of research purpose. So, in that case it may not be an

issue, but again the question lies whether such couples or such women are informed about the use of such embryo in this kind of the research or not.

So, but still it would not directly harm the embryo as the earlier cases and this kind of view was also endorsed by the former first lady Nancy Reagan and the US Senator Orrin Hatch in the United States. So, if you see the political or the debate surrounding these kind of human embryonic stem cells, it is worldwide.

Now, irrespective of the country whether you say it US where these research in that area has begun quite early in during the 1970s itself, but still then if the debate is still going and now, we have lot of regulations or lot of streamlined process. So, these kinds of questions can be answered in a proper scientific manner.

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New embryonic stem cell lines from frozen embryos

- Frozen embryos remaining after they complete their infertility treatment. Are donated for research rather than giving them to another couple for reproductive purposes or destroying them.
- Ethical concerns with respect to donated frozen embryo:
 - informed consent from the woman or couple donating the embryo,
 - consent from gamete donors involved in the creation of the embryo, and
 - the confidentiality of donor information.

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So, instead of directly harming a embryo inside the womb of an women, so, there is the alternate way is to use the new embryonic stem cells lines from the frozen embryos. So, the frozen embryos are generally preserved in biobanks or as I was mentioning in the in vitro fertilization clinics. So, after the treatment or procedure of the infertility treatment these frozen embryos are kept in those kinds of clinics.

And generally, they are donated for the research instead of using that for another couple. However, again the use of such donated frozen embryo may raise certain ethical issues. First

like, whether or not the informed consent from the woman or the couple donating the embryo has been taken or not, are the couple couples informed about the possible usage or the way the embryos are going to be used whether proper informed consent has been taken out or not, whether they realize that what kind of research is that? So, that is a big question.

And then consent of the gamete donors involved in the creation of the embryo. So, if we have the gametes like the sperms or the eggs then individual consent has been taken or not. In there has been studies or the surveys where in many cases the woman did not like that their eggs should be used for any kind of the research whereas, in some cases the embryos donating the embryos for biological science research has been favored in some countries.

So, there are different views depending on their religious belief or depending on their personal choices. And further the issue of the confidentiality is also a major concern here. Because if the identity of the donor is revealed, so that may lead to a problem for the donor or may be a threat from the groups, who believe that destroying an embryo for this kind of research purpose is not good. So, the ethical concern with related to the frozen embryos is also prevalent.

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Ethical concerns about oocyte donation for research

- **Medical risks of oocyte retrieval;** ovarian hyperstimulation syndrome, bleeding, infection, and complications of anesthesia... careful evaluation needed
- **Protecting the reproductive interests of women in infertility treatment:** reproductive needs must be prioritized
- **Payment to oocyte donors:** payment to oocyte donors in excess of reasonable out-of-pocket expenses is controversial
- **Informed consent for oocyte donation:**
 - Poor Understanding of the informed consent process

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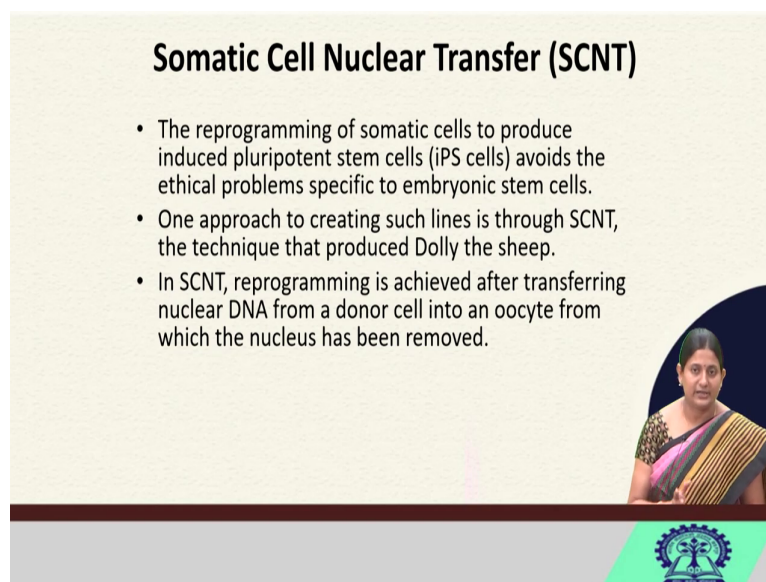
And sometimes there are further ethical concerns related to the donated oocytes ok. So, maybe for some woman participants agreed to donate the oocytes for further research, but

again the process of taking out the oocytes from the body is a very risky process. And it may have many side effects as well as effects like this ovarian hyper stimulation syndrome, it may lead to bleeding or other infection or complications of anesthesia. So, if something like this is has been carried out it has to be done properly and it should be carefully evaluated.

And then because sometimes we have come across the unethical practices in the scientific world, so, care must be taken to protect the reproductive interest of such donors or the woman in the infertility treatment. So, the first reproductive needs must be prior prioritized rather than prioritizing the extraction of the oocyte for the scientific or research purpose.

Then the proper informed consent for the oocyte donation. In many cases the woman does not understand what is this informed consent or why this thing has been taken out or what is the purpose of this kind of the research and so, it they have to be properly understood regarding the usage of the oocyte and how it is going to be used in the research and what are the future consequences or in what way those are going to be used.

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Somatic Cell Nuclear Transfer (SCNT)

- The reprogramming of somatic cells to produce induced pluripotent stem cells (iPS cells) avoids the ethical problems specific to embryonic stem cells.
- One approach to creating such lines is through SCNT, the technique that produced Dolly the sheep.
- In SCNT, reprogramming is achieved after transferring nuclear DNA from a donor cell into an oocyte from which the nucleus has been removed.

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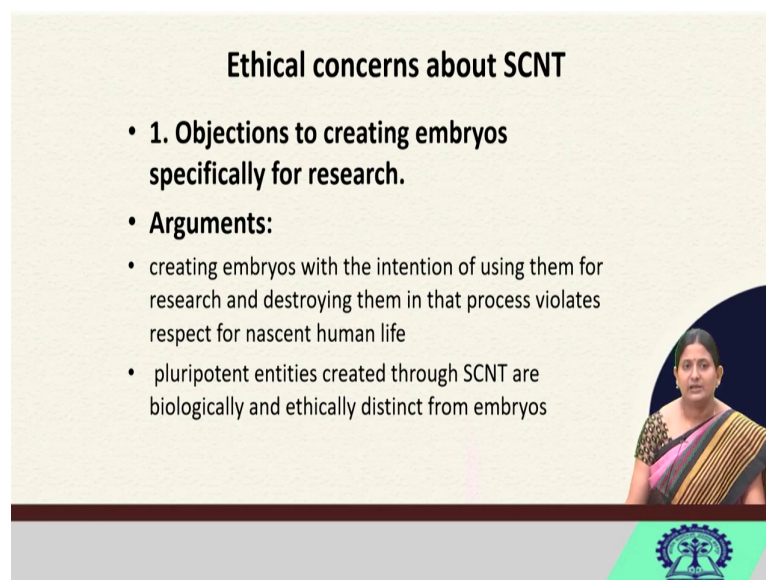
So, with related to the embryonic stem cells these are the whatever we have discussed so far were the major issues like weather from the frozen embryos or for the donated oocytes or directly from the human embryonic 4 day old or 6, 7 days old embryos. So, when it is coming to the embryo or the fetus? So, that is directly raising an ethical question.

So, scientists have been working in developing the stem cells like these embryonic stem cells or the pluripotent stem cells which has the ability to develop into many different kinds of the tissues from the somatic stem cells itself. So, there was a popular example of the sheep which is known as the named as Dolly.

So, the Dolly sheep was a clone of their mother sheep and if you know though that kind of technique where the somatic cells where the nucleus of the somatic cell has been inserted into a fertilized egg is known as the somatic cell nuclear transfer. So, it is basically the reprogramming of the somatic cells to produce the induced pluripotent stem cells. Means, the it is the pluripotency has been induced by some kind of genetic interventions.

And this is one of the way the ethical consideration to the related to the embryonic stem cells is trying to be or has been avoided. So, this process of the somatic cell nuclear transfer is quite prevalent in many of the animal breeds like sheep is another example, Dolly was a popular example. But, the nuclear DNA was transferred into oocyte from which the nucleus was removed, but when it comes to the human again it raise a several questions.

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Ethical concerns about SCNT

- **1. Objections to creating embryos specifically for research.**
- **Arguments:**
 - creating embryos with the intention of using them for research and destroying them in that process violates respect for nascent human life
 - pluripotent entities created through SCNT are biologically and ethically distinct from embryos

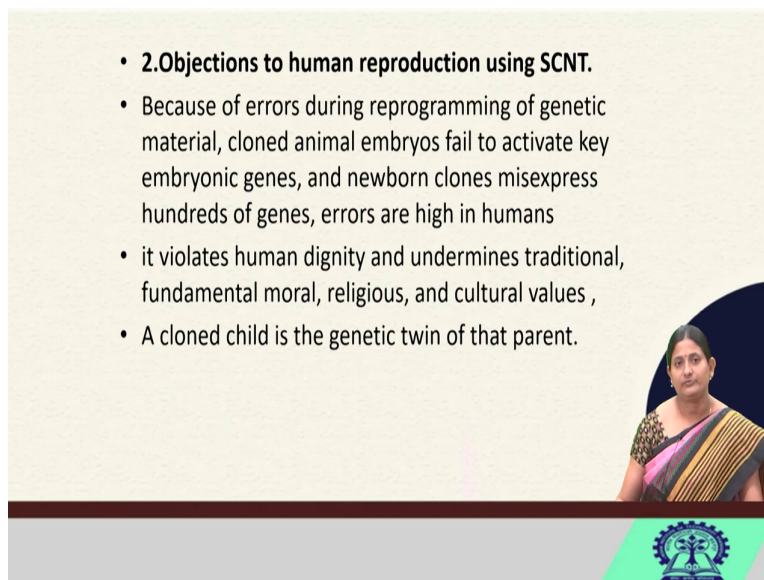
Like, there are again different kinds of arguments. Again, creating the embryos with the intentions of using them for the research and destroying them in the process is it really required and does it taugt violates the respect for the nascent human life? So, you are

deliberately creating a human embryo and destroying it for your scientific endeavors. So, it is a kind of violation to the human value.

Then another issue is that another issue is that the pluripotent entities which are created through the somatic cell nuclear transfer process are biologically and ethically distinct from the embryo. So, here what happened is the, so, the nucleus of a somatic cell has been incorporated into the oocyte. So, it is not equivalent to the embryo which is generally developed to the normal process.

So, they say, so, these are two different kinds of the cells. So, that should not be a problem. It is about solving certain scientific or certain issues in the biomedical research. So, it should not be taken as same or at par with the embryonic stem cell research.

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- **2. Objections to human reproduction using SCNT.**
- Because of errors during reprogramming of genetic material, cloned animal embryos fail to activate key embryonic genes, and newborn clones misexpress hundreds of genes, errors are high in humans
- it violates human dignity and undermines traditional, fundamental moral, religious, and cultural values ,
- A cloned child is the genetic twin of that parent.

And when it comes to use of this process in the human reproduction again there are many objections. So, one of the objections is because of the possible safety concerns. So, when someone is trying to reprogram this genetic material from a somatic cell to that kind of cell, so, that may lead to the, faulty expression of different kinds of the gene.

So, there may be hundreds of the genes which are mis expressed. So, it may lead to the development of certain undesirable proteins or certain undesirable functions which is very harmful to the human beings and it may generate lot of errors in the humans. And the chances

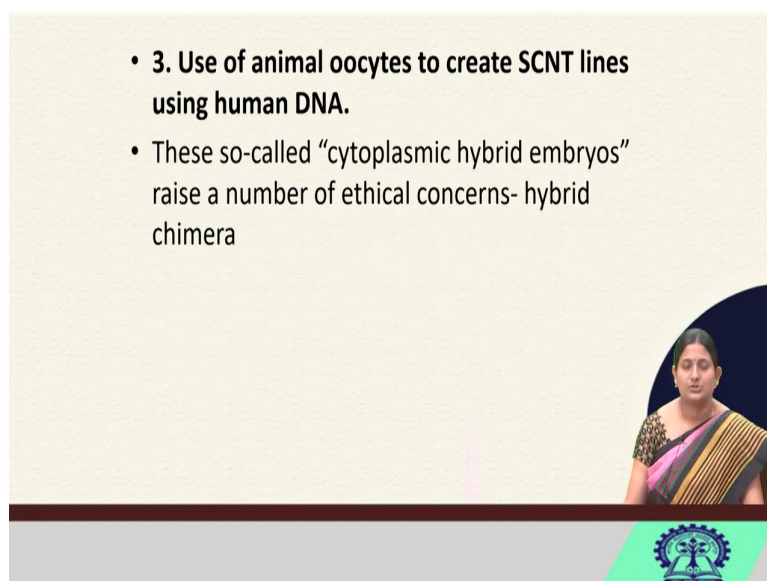
of this kind of errors like this misexpression of the genes are very high in case of the in humans rather than in animals.

And somewhere it also violates the human dignity or it undermines the traditional or fundamental morals or religious or cultural values of the human being when someone is approaching or using this kind of process. And the other issue is that in many case the cloned child like this Dolly sheep. So, if it is in case of the human, so, it would be considered as a twin of that parent because the genetic material becomes the same because it has been taken from the body of that mother or that cell.

So, when you are again incorporating that into the oocyte and it is developing into the full fledged human being, so, it is basically a genetic twin. So, that emotional attachment or that value or the feeling that a couple gets while considering their child or when the child is born is not equivalent to the clone child.

So, these are the few objections which are also being taken to the use of this somatic cell nuclear transfers process in for developing the cloned individual. However, if you see there are examples in the animal. So, cattle industry or sheep industry that has been tried, but there the ethical issues are not that, what you called not raised in that way how it has been raised in the case of the humans.

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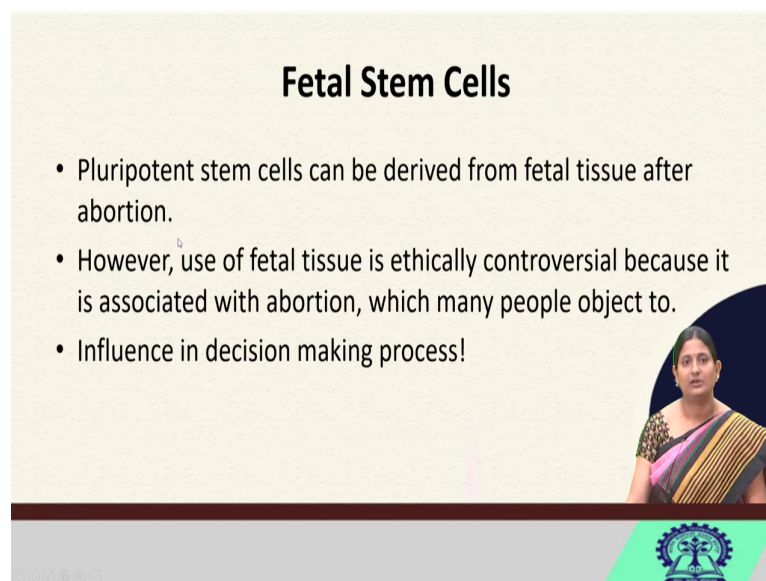


- **3. Use of animal oocytes to create SCNT lines using human DNA.**
- These so-called “cytoplasmic hybrid embryos” raise a number of ethical concerns- hybrid chimera

So, also there are 3rd kind of issue where the animal oocytes are using the human DNA. Means, instead of the like the earlier example here the human DNA is injected into the animal cell. So, it may lead to the development what we call as the cytoplasmic hybrid embryos and which is called the hybrid chimeras what you called mythological characters of the beast or other character were nonhumans like as mixture of the human with the animal.

So, that kind of things generally becomes a concern when we come to this kind of research. But anyway, but in case of the animal like we have known the example of the mule or other animals where it are a kind of a hybrid chimera, but when it comes to human DNA into the animals then it is not ethically acceptable by many part of the society. So, this is also a kind of issue which comes to forefront when we deal about the stem cell research.

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Fetal Stem Cells

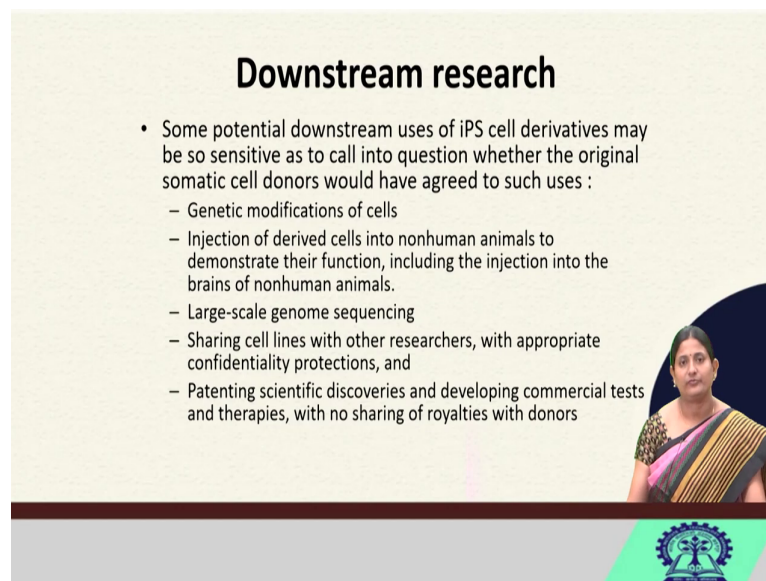
- Pluripotent stem cells can be derived from fetal tissue after abortion.
- However, use of fetal tissue is ethically controversial because it is associated with abortion, which many people object to.
- Influence in decision making process!

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So, one of the simplest way to derive this fetal stem cell is like, if a natural abortion occurs then the pluripotent stem cells can be derived from the fetal tissues after that abortion process. Again, since it is associated with the abortion process again it is an objectionable to many groups and so, it because it may lead to deliberate abortion or a money making process.

You never know how much incentive is been given or other things. So, that is again a controversy here. So, whether abortion should be allowed or not allowed and the fetal tissue can be used in the stem cell research or not.

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Downstream research

- Some potential downstream uses of iPS cell derivatives may be so sensitive as to call into question whether the original somatic cell donors would have agreed to such uses :
 - Genetic modifications of cells
 - Injection of derived cells into nonhuman animals to demonstrate their function, including the injection into the brains of nonhuman animals.
 - Large-scale genome sequencing
 - Sharing cell lines with other researchers, with appropriate confidentiality protections, and
 - Patenting scientific discoveries and developing commercial tests and therapies, with no sharing of royalties with donors

The slide features a portrait of a woman in a sari on the right side and a logo at the bottom right corner.

So, not only the use of the embryos or the stem cells or the pluripotent for the derivation of the stem cells is an issue now we have discussed the multiple ways through which the stem cells can be recovered from direct from the embryo or fetal tissue. After the abortion or induced pluripotent stem cells where a different genetic manipulation or interventions has been done to make some adult stem cells or the normal stem cells into a pluripotent stem cell.

So, again those are the issues at the stage where the stem cells is being developed and used for the biological research or means the first stage of isolation of the stem cells. But again, the problem is not only that first stage of the process, the in the next downstream research process it also it is also a major problem. So, we have to now see what kind of usage this stem cells might have or the induced pluripotent stem cells might have and what kind of sensitive questions can be associated with those usage.

So, when the pluripotent stem cells are derived from some donors or from any other process, so, generally they would be used in the future genetic modification of the cells or they would be used in deriving like using that cell which would be injected to certain non human animals to demonstrate the various functions or it may be injected into the brains of the non human animals to see how it is affecting the development of the neural cells or other things.

Then it might be used in the largescale genome sequencing to understand the development of the cell line and how where the fault. So, that the whole cell biology or the cell differentiation process can be understood at the fundamental level to diagnose proper diagnosis of the disease or the treatment of the disease.

And further the patenting issue or intellectual property issues develop related to the discoveries or the inventions related to the commercial test or the therapies which are now produced through the embryonic stem cells and the future income and the royalty sharing. So, these are the future or the downstream research process which may arise with the help of the stem cells.

But, again the donor or the persons from whom the stem cells are being received they might not agree to use their cells or the body parts to for use in those direction. For example, when there is large scale genome sequencing, so, one may able to understand what kind of genetic threat or probable disease he might be getting in future or when the cell lines are injected into certain non human animals then they might have certain religious reservation or they should they may not like it.

Or when it is genetically modified or further manipulated that may be may not be acceptable to certain individual who have agreed to give the embryonic stem cells or the stem cell. So, even at the later stage also the informed consent process or the normal ethical considerations has been majorly seen.

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hESC research in US

- In 1974, the Congress Banned nearly all federally funded fetal tissue research until the National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research, established by the National Research Act, devised guidelines for it.
- In 1975 an Ethics Advisory Board was established, whose guidelines were to look into the issues regarding fetal and fetal tissue research that originate from abortions.
- In 1980, President Reagan Killed the Ethics Advisory Board, leading to a de facto moratorium halting federal funding of human embryo research due to the EAB's disbanding.
- In 1988, though, the Federal Panel Approved Funding of Embryo Research after a lengthy debate on its merits and demerits.
- In 1990, President George H.W. Bush Vetoed the Bill Lifting Moratorium, thus denying funding to stem cell research.



So, these are the few issues in general I wanted to discuss regarding the or the ethical issues with respect to the embryonic stem cells and if we go the earlier one of the developed nations like United States, where the embryonic stem cells has started early in the 1970s itself in.

So, if you see the evolution or the time line how the things has been perceived there. We will find that in as early as 1974, initially the till then it was federally funded at the all these embryonic stem cell research, but the Congress banned nearly all federally funded fetal tissue research in 1974.

And until the National Commission for the Protection of the Human Subjects of Biomedical and Behavioral Research was established by the National Research Act and they devise guideline for how to go about this embryonic stem cell research. Then in 1975, Ethics Advisory Board was established which basically a body which allowed the functioning or allowed permitted gave permission for this kind of the research.

Again in 1980, President Reagan Killed this Ethics Advisory Board which laid to the de facto moratorium halting the federal funding for the human embryo research. And again in 1988, there was lot of debates regarding the merits and demerits of the human embryonic research and finally, in 1990 by President Bush the all the federal funding to the stem cell research was denied.

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- **Finally in 1993, President Clinton by an Executive Order Lifted the Moratorium** but subsequently again reversed it in 1994 due to extensive public outrage and pressure.
- **In 1995, the Dickey-Wicker Amendment**, named after its sponsors Jay Dickey and Roger Wicker, a Congress measure which prohibited the use of federal funding to embryonic research purposes as the use of human embryos was seen as a violation of human rights, was enacted.
- **In 1998, James Thomson Isolated Human Embryonic Stem Cells**, This discovery also initiated the ethical debate on human embryonic stem cell research because his team derived the stem cells through a process that destroyed human embryos.

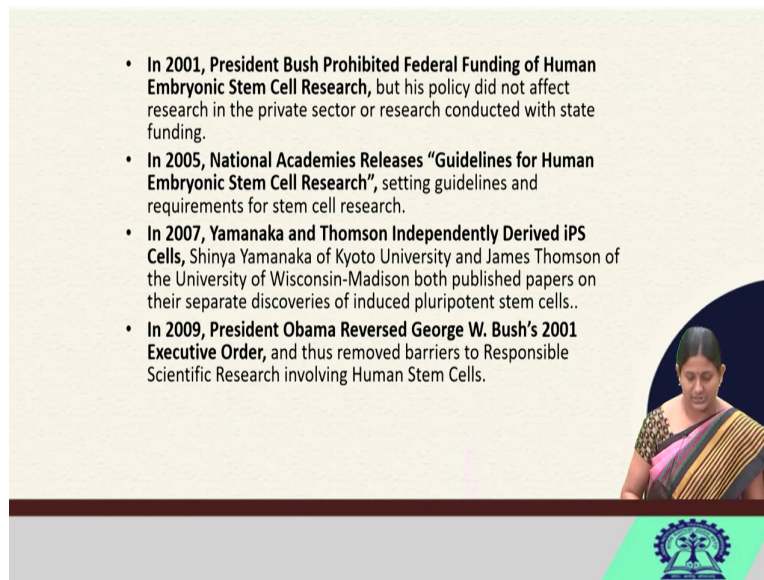


And there are further major few changes has been also done after that, but the major change came in 1995 which is known as the Dickey-Wicker Amendment which is named after the sponsors Jay Dickey and Roger Wicker. So, basically with this amendment they prohibited the federal funding towards the embryonic research for all the purposes where the use of the human embryos was seen as a violation of the human rights.

So, after this Dickey-Wicker Amendment if any of the embryonic research where the embryo has been destroyed or you there is a use of the human embryo then it did not allow the funding of such kind of the research. So, till the time the embryonic stem cell research was basically based on the extraction on the embryo extraction of the cell lines from the human embryo itself.

But, in 1998 James Thomson isolated the first human embryonic stem cells and this discovery again initiated the ethical debates and how the human embryonic stem cells research is required or is really as needed or not because again it was derived through a process where it has destroyed the human embryo.

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- In 2001, President Bush Prohibited Federal Funding of Human Embryonic Stem Cell Research, but his policy did not affect research in the private sector or research conducted with state funding.
- In 2005, National Academies Releases "Guidelines for Human Embryonic Stem Cell Research", setting guidelines and requirements for stem cell research.
- In 2007, Yamanaka and Thomson Independently Derived iPS Cells, Shinya Yamanaka of Kyoto University and James Thomson of the University of Wisconsin-Madison both published papers on their separate discoveries of induced pluripotent stem cells..
- In 2009, President Obama Reversed George W. Bush's 2001 Executive Order, and thus removed barriers to Responsible Scientific Research involving Human Stem Cells.

In 2001, President Bush prohibited the federally funding schemes for the human embryo embryonic stem cell research, but again it did not affect the research in the private sector. And the research was conducted with can be conducted with the state funding. In 2005, the National Academies Releases; release the guidelines on the human embryonic stem cell research and it basically set the guidelines and requirements for the stem cell research.

And the major breakthrough came in 2007 where two independent scientist Professor Yamanaka and Professor Thomson. So, they independently derived this induced pluripotent stem cells and they separately discovered it. So, after this induced pluripotent stem cells like outside the human body when these with the help of certain genetic interventions the stem cells are converted into the pluripotent stem cell.

So, that gave a big breakthrough where the use of the human embryonic stem cells can be reduced. So, again 2009 President Obama reverse the Bush's order George Bush order for stopping the federally fund and they tried to remove the barriers for the responsible scientific research involving the human stem cell.

So, there are many changes because all these are politically debatable issues, so, linked with many other religious and as I said political debates. So, there has been changes according to the situations.

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- **Sherley v. Sebelius**
- **In 2012, the Court of Appeal upheld federal funding of embryonic stem cell research,** a Senior US appeals court ruled on August 24, 2012 that the US National Institutes of Health (NIH) is legally able to fund research based on human embryonic stem cells.
- The decision was made by a three-judge panel of the US Court of Appeals for the District of Columbia Circuit and upheld a 2011 decision by a lower court, which found that the NIH's funding of the research was legal despite the 1996 law (Dickey-Wicker Amendment), passed by Congress, which previously forbade funding research in which human embryos are destroyed.



One of the important decisions, which like this Sherley versus Sebelius. So, here this was again a case related to the issue of federal funding towards the embryonic stem cell; embryonic stem cell research. So, in this case if court of appeal upheld this federal funding of the embryonic stem cell research. So, basically in this case the decision was made by a three judge panel.

So, there they found that this NIH funding towards the research inspite of this other amendment which is the Dickey-Wicker Amendment, where it said that the research where there is a destruction of the human embryo or use of the human embryo directly should not be funded. But, here in this case the research was not directly using the human embryo and so, it is not coming under the purview of that and it should be federally funded.

So, that is why, so, there has been number of issues moral ethical consideration related to these embryonic stem cells though it has a bigger potential in treating various diseases, but because of these ethical issues so far we have not been so successful in this arena. In US there has been some clinical trials with the stem cells therapy. Already one or two products has been approved by the US FDA.

But, in other countries because of these ethical issues only it has not been successful and also there are safety concerns definitely. But, overall, in stem cell research and particularly human

embryonic stem cell research the ethical issues are a major setback or major controversial point which is stopping from going easy towards in compared to the other biomedical field of research.

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So, these are the few references, you may go through it. So, with this I am just concluding the portion on these stem cell ethical issues in general. In the next class we will discuss about the Indian perspective towards the stem cell research.

Thank you.