Bioengineering: An Interface with Biology and Medicine

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Lecture - 28
Principles and Application of Animal Cloning

Welcome back to the book NPTL course on Bioengineering an Interface with Biology and Medicine. In the last lecture, we talked about some basic concepts of development. In the same theme today we are going to continue studying about cell reprogramming. How cell can be reprogrammed? And we have tried to do some elegant experiment in this area where people have try to understand how cloning can be performed at animal level and for different type of purposes both for a production as well as from the therapeutic point of view.

In today's decision in today's lecture I will continue and talk to you about some successful experiments in the areas of induced pluripotent stem cells making as well as there are many cloning attempts which has resulted into some of the major breakthroughs in the field. Some of them are related into some big scientific ground breaking research and got noble prize. Some of them also resulted into the scientific scandals and got some punishment.

So let us continue discussing about cell reprogramming. All right, let us shift gear and move onto second topic which is Cell reprogramming and Cloning. Cloning I think briefly talked in a form of context of DNA cloning. How to make multiple copies of DNA? Not in great detail but while I was talking to about rule of biotechnology; in which way you can make multiple copies of the genes which could be favoring certain you know properties that can be used for recombinant DNA technology.

I had talked to you briefly about it. Let us look at some of the animal and organism cloning part and this part look much more interesting, fancy, you know scientific fiction type of idea.

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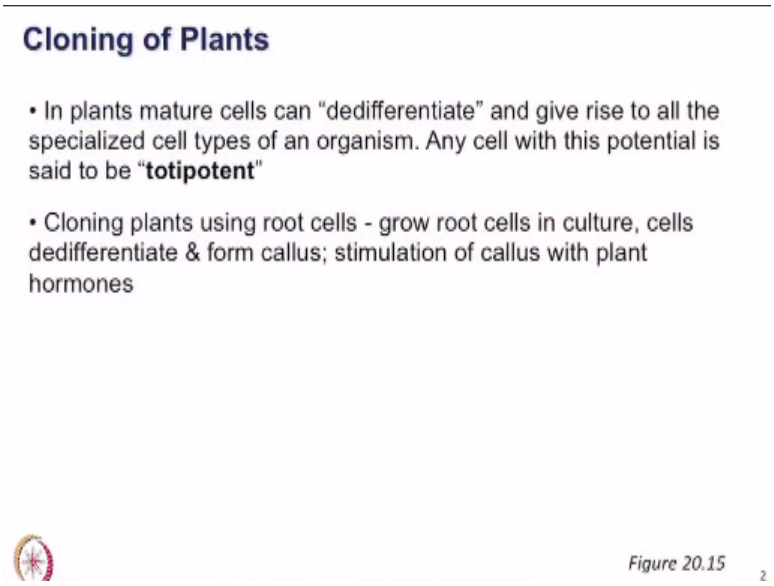

But before that even cloning also can happen in the plants because plant cells have much more ability to make totipotent cell, it means the cells have property which they de-refresh it into any type of the cell if you just provide them right hormone and right medium conditions. Let us see this experiment.

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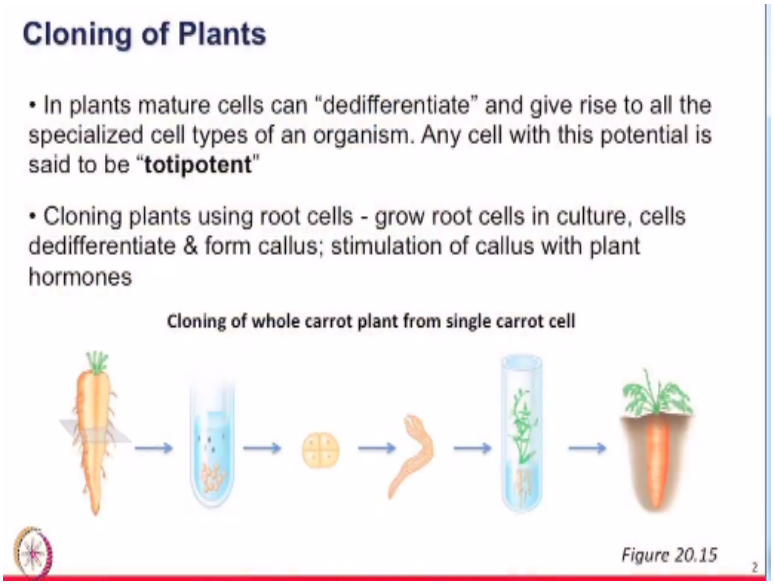

This is the carrot, if you are taking this small piece of carrot root, putting it from nutrient medium you can see that you know the cells are dividing and now a small embryo was developing from in it. And if you put now it in again some nutrient medium which contains Cytokinin and Gibberellic acid etcetera those hormones, now it can form the root and shoot and it can result into full carrot.

So plant cloning of course you know is very useful from agriculture point of view. Many times you would have seen that people have taken a small part of a given plant and may use those plants to now you know further grow and put in a different field, right. And they actually result into new trees or new plants.

So there are in fact some plants which I do not know whether you have noticed any or not like if the leaves even fall down from them and if you know from the surrounding of those soil area even though leaves will result into certain type of another tree. You know any example? Right. So some of the banyan tree and many of the other examples are there which do follow this kind of pattern.

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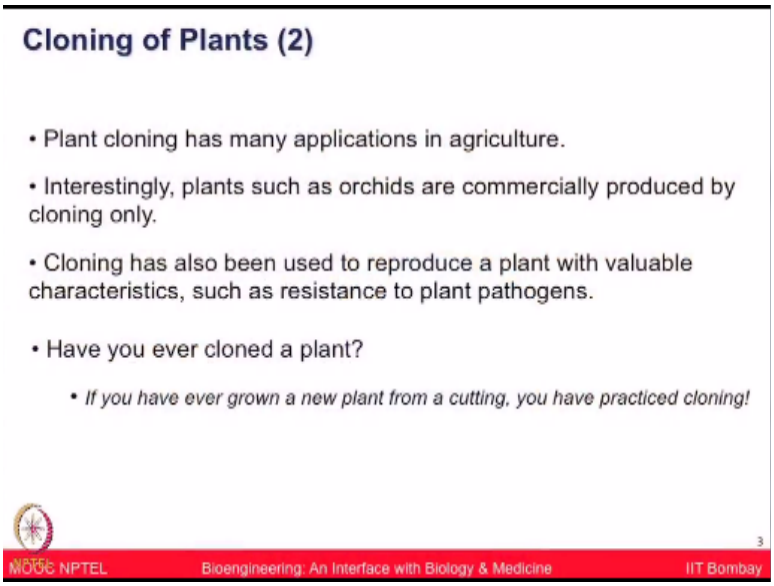

And cloning in general plants are much more flexible having much more totipotency in that way that they can modify themselves and they could actually result into the full new plantlets. So if you have not cloned a plant of course that is something small experiment should be tried which you can do yourself; it is not going to harm you. Let us think about the animal cloning which is much more tedious part, process.

Many things have to be controlled for full animal to be made if you want to try it out.

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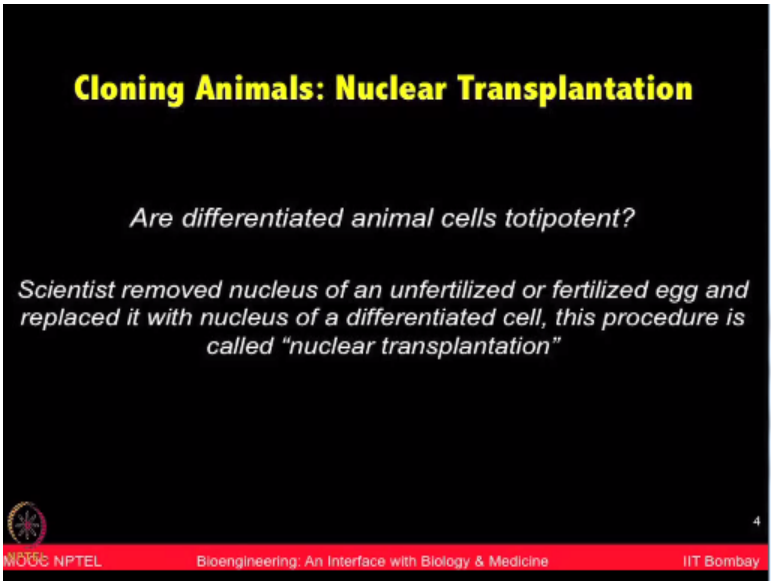

So Nuclear Transplantation is one of the concept which aims to look at whether similar type of plants type of concept can be used for the animal cell. Are the animal cell totipotent? Can they be converted into any type of cell which you want? So you know, scientist have tried to do the experiments, they used some of the fertilized eggs as well as some of the fertilized egg too that they took, they try to replace it with the nucleus of the differentiated cells which are you know much grown cells.

And then try to do the experiment to test out the hypothesis, can the nuclear transplantation may happen. So the possibilities are from this hypothesis that if nucleus from the differentiated donor cell retains its full of the genetic information then it is should be able to direct the development and give rise to any type of tissue type. It might be very complex right now. Let us think about this hypothesis, it is much more somatic form.

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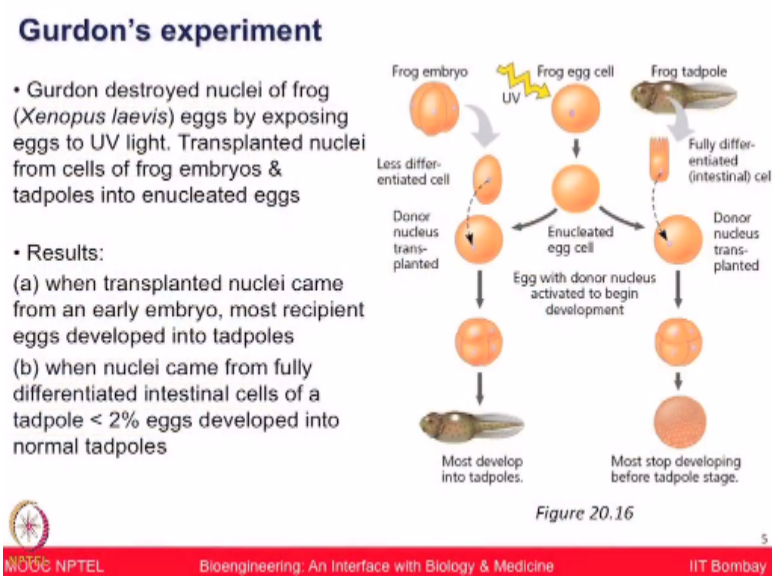

Think about experiment which was done 1960s. Intention was to look at whether animal cell have the similar type of totipotency properties and what type of animal cell may have those properties. So John Gurdon, he did experiment in 1960s using frog eggs.

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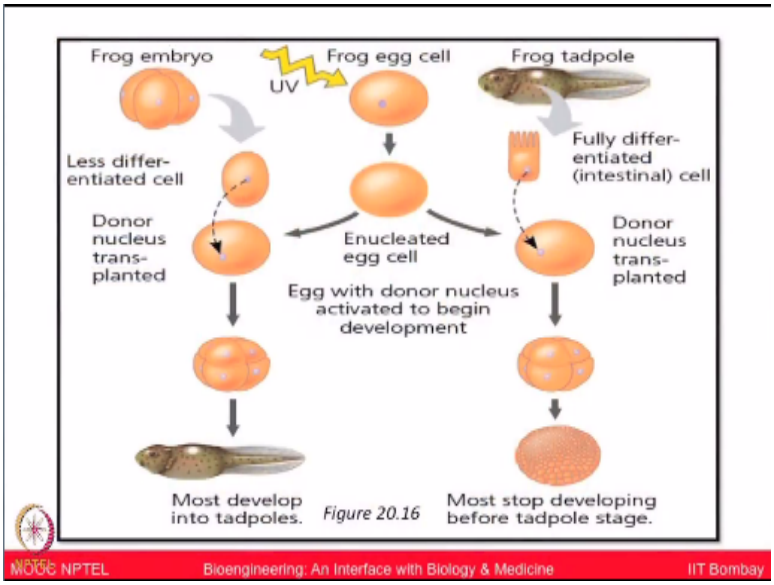

So he took the frog egg cell and did the UV radiation to remove the nucleus from this frog egg. Now what you get is enucleated or nucleus removed from the egg cell. So just pay attention to the experiment and then you will be clear about the experiment. So now you have this nuclei egg cell and you are trying to add a nucleus you are doing the nuclear transplantation from one of the two conditions.

Condition one is you are taking an early stage of the frog embryo taking some cells from it and now you are trying to you know use this particular egg cell environment and use those nucleus to fuse the thing together and see can it now develop into the full embryo, that is one possibility. Second possibility they took the developed cells you know like skin cell or a intentional cell not the embryonic cell but the developed tadpole developed cells at the in intestine layer or the epidermis kind of layers.

And from those they took out the nucleus now again and trying to transplant into this particular egg cell again. So this possibility when they tried out they you know only 1% or 2% of them resulted into the successful embryo and it did not result into the full tadpole whereas with this experiment when they use the early embryonic stage of the frog cells then it resulted into the successful transplantation and many of them developed into the tadpole larva.

So it just conveyed them it is possible to use the right stage of the animal cell for the nuclear transplantation to happen and if you can use some of the early embryonic stage cell which are less differentiated cell then probably they can achieve the totipotency potential. So this experiment was you know just imagine thought and done in 1960 and with a very limited technologies available with just some good hypothesis and good concepts which they tried out.

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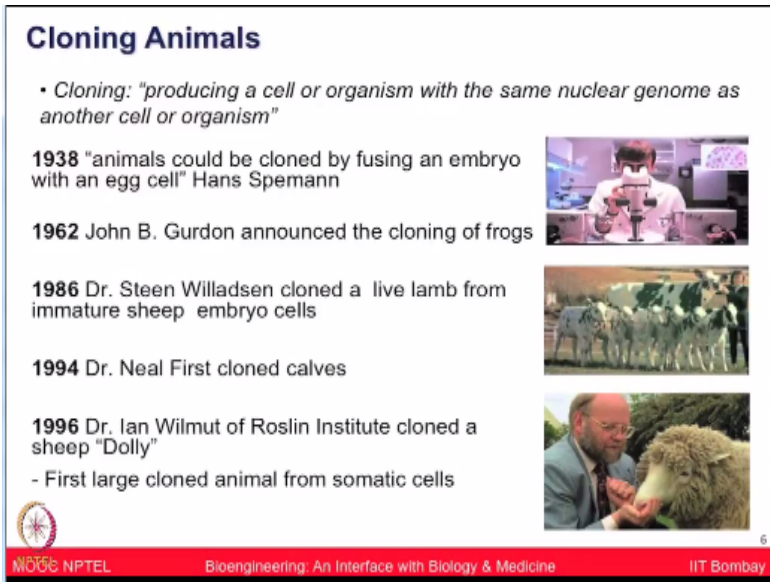

Based on those many people have started trying out many type of animal cloning, right. Let me take help some of you to read rather than I talk about it. Okay, so this cloning of frog was one of the very successful experiments being done and many people started following; can we do animal cloning on different type of animal as well because frog is not something which can give you any commercial output?

Think about can you make, you know cloning of the dogs, cloning of the cow; cloning of sheep all of them have lot of commercial values, right. The high breed of these animals if you can make multiple copies of their; with the cloning process then probably you will have lot of commercial value. So many people started venturing into the cloning of animals different type of animals and then, you know I am not going to ask you questions about the scientist name who did that but just trying to show you the progression that from

1960 onwards many people have tried to do cloning of animals and some of those are listed here like after Dr. John B. Gurdon did the cloning of frogs; 1996 Dr. Steen Willadsen tried cloning of the immature sheep; 1994 they tried the cloned calves Dr. Neal first and 1996 Dr. Ian Wilmut of Roslin Institute in UK, he did a very successful experiment first time from the body cell the somatic cell they made the Sheep Dolly.

I am sure many of you would have heard at least in one of the interesting story format about the success of Dolly. So this is one of the success examples because you are now trying to reprogram even some of the somatic body cell and trying to develop into the full animal from that. So reproductive of mammals it is something which higher lot of both commercial aspects, values and limitations and ethics and of course you know danger of going into wrong hands and doing something wrong, right. So it is much of the issue of a debate.

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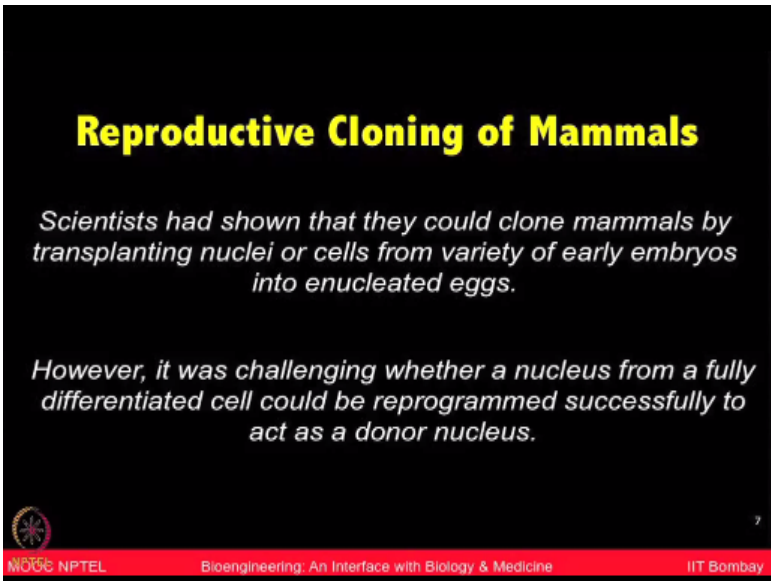

But it is a fact that is people have now mastered the technologies and they can do these cloning processes. So scientists have shown that you know they could clone mammals by transplanting nuclei from the early embryonic stage; we have talked about the original experiment of Gurdon and then many people have tried in different other animals from the early embryonic stage you can take those cells you can transplant them and you can use them as a for the cloning purpose.

However, it was challenging that whether the nucleus from the differentiated cell or the matured cells or the body cells whether that could be use for the reprogramming. Because even Gurdon when he showed the develop tadpole larva from its intensive epidermis they were not able to succeed into cloning process, so this remained a still challenging that whether you can use you know the normal body cell the somatic cell and use those for the nucleus transplantation experiment.

So that is where the scientists actually transformed into reality and the scientist Dr. Ian Wilmut of Roslin Institute the first time claimed that they can now make the full large animal a sheep by using the somatic cells. And this experiment has you know lot of value because they are first time able to achieve dedifferentiation of these donor cells just by taking the memory cell of the sheep. And in many ways they have mastered understand about the cell cycle.

They know that at which stage you can keep the G1 stage controlled where you have to make it before G1 there is a G0 stage when you can you know can keep the cells in the stage in the dormancy when you can trigger the factor for it you know, now turned into proper division, all of those were so well understood that now they can play with the conditions play with the nutrients and then you can able to culture the memory cells and trying to use those for the cloning.

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Here Dr. Ian Wilmut is shown and for a delight I had also some interaction with Dr. Wilmut when I was at Harvard. So the experiment what it happened, in this experiment they took one of the sheep from which they took the memory cells.

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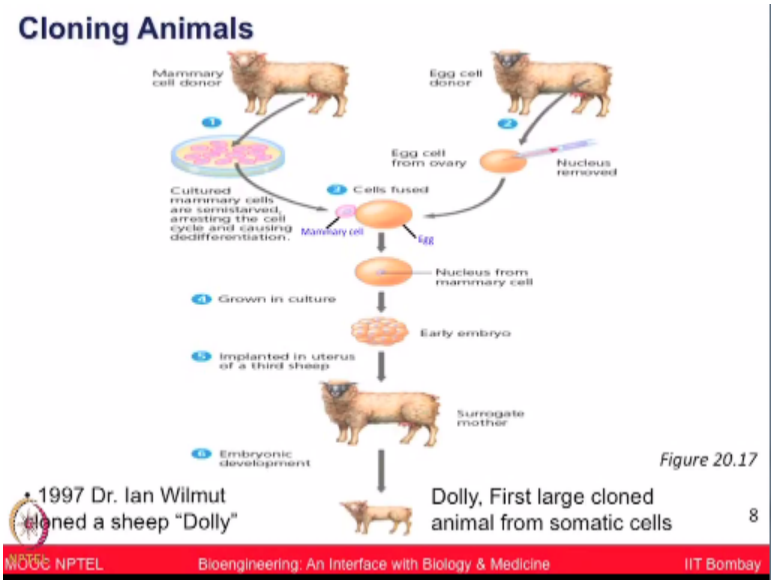

Just took the memory cells which is you are not taking any genetic content of it you are just taking the; not the gambit just taking normal somatic cell memory cell in this case. And there you took another donor sheep from which you are taking out the egg cells. So from this particular sheep now you have removed the nucleus out you got enucleated cell and now from the memory cell you are taking out the nucleus. You want to transplant. And for this process we have tried many things.

Sometimes even just a electric shock can help to facilitate the fusion of this particular cell with the nucleus. And you need many attempts you know even they have tried probably 100s of attempts of those only one or two were successful which resulted into this kind of cloning. So it is not so guaranteed process that it will always happens. But after many attempts they were able to succeed into some of the cell which could incorporate and grow into the early embryonic stage.

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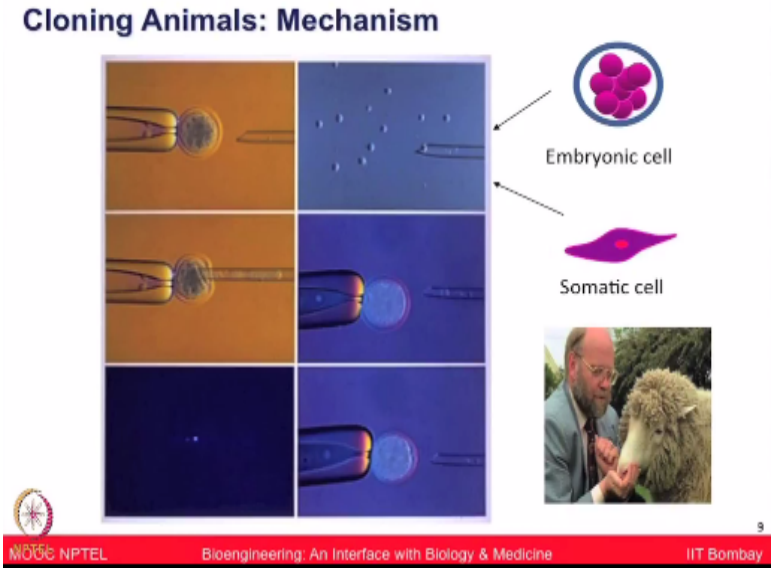

Then they used third surrogate mother not these two but a third surrogate mother now where they have transplanted this embryo which resulted into the Sheep Dolly. So it looks like a scientific fiction but they actually did it and they showed first time that it is possible to do the using somatic cell you can do the dedifferentiation and you can do the cloning.

So again you know this just needs very basic technique; it does not need not too much of high gadgets and technologies, it just need you know understanding very well of how well you can take out these nucleus from the ova how well you can culture them; how well you can control them and then you can result into the full embryo development. A question there, yes. That is right. I think that is very interesting observation made. They could have used any of these two, right? They could have used any of these two to you know for further growth.

What in this case they wanted to ensure that their cloning has actually happened and it is actually not coming dictated by any of these two. So if you are using the third mother now then you can totally claim that all the DNA content coming from the other two still having a potential to give rise to a new embryo, so that was the good reaction of thinking about taking a surrogate mother. But of course this could have been done in the same sheep as well.

So whether cloning is you know such a full proof process or is it that like you know photocopying machine where you can make the photocopies of animals; you can keep producing whatever animal you like you know having commercial value then you can do anything for that matter, right. But cloned animals are now always perfect. They do not look exactly same.

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And these kinds of observation people have made for many of the cloned animals including cows, including cats. Let me show the interesting example here.

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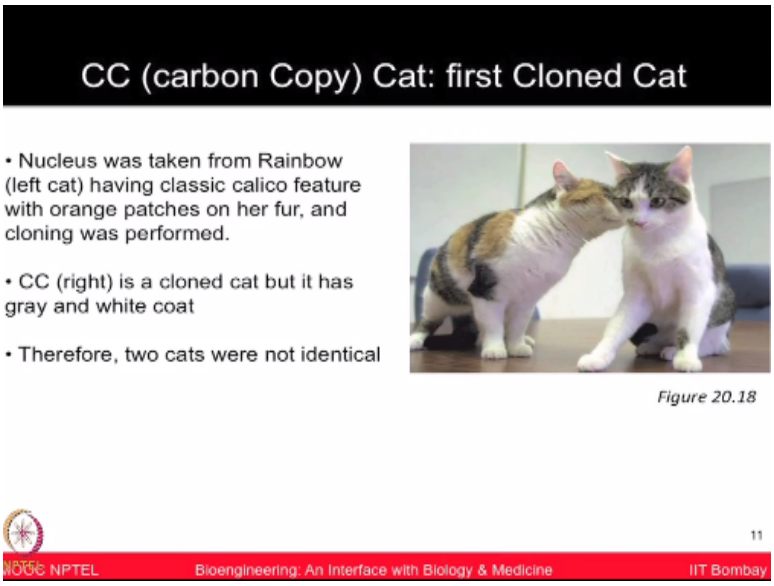

Figure 20.18

This cat is known as Carbon Copy a CC cat. It is also cloned cat. Now the two cats ideally should exactly look same because they are cloned copies carbon copies, but one of the cat has you know some of the light yellowish of the fur were other one having grayish color. So whether this is matters much or not but ideally you do not have the same appearance. So while the genetic content could be still same and have been derived from the same cloning process but they are not exactly identical, right.

So that leads you know some possibility that irrespective of how you are overcoming the, you know the natural laws of development process, but there might be some random events are happening especially you know chromosome inactivation etcetera which could be leading towards along with many environmental factors which could be leading into different type of embryonic development for the different clones to happen.

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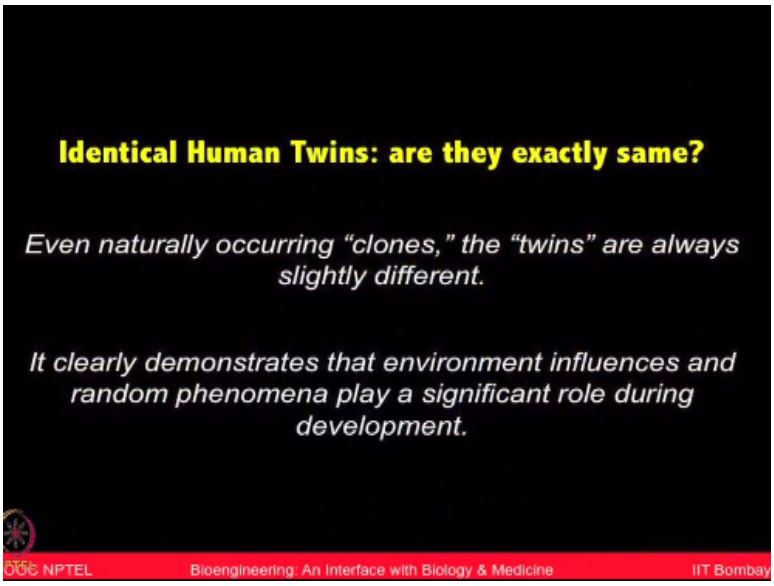

Let us look at you know Identical Human Twins example. So I am sure you would have encounter or seen some individuals were twins. And they look very similar, you know they are very close in appearance but they do not exactly same. And even they are you know kind of nature wise and their property wise they cannot be exactly the same. So it means it is not only the genetic makeup it is also important that in which environment they have been grown.

And what kind other factors especially epigenetic factors which are also purely important along which a genetic factors, how they influence the development process. So therefore, two individuals' even two twins or two clones cannot be exactly identical. I think that has been one of the concern as well that you know if you are planning to have at the commercial level at the very large scale level how perfect the technology is.

Just imagine that you know you are doing mass production of certain you know leather or mass production of you know various products right. Can you do same way of mass production for cows; can you do same mass production for any of the animal which you want; theoretically, yes you can but because it will not have success of producing everything perfect people are not allowed to do those things at that level.

So there has been many observation that many of the cloned embryos they initially they look normal but after some time that have encountered certain type of you know defects. Especially in

apparent case of Dolly which was the example which we talked, even Dolly dead in 6 years' time which is not the right age for dying for a sheep. And people may feel that you know probably is the time that when the DNA was taken and if the age being counted from that DNA because that DNA from that sheep would have already taken 20 years probably.

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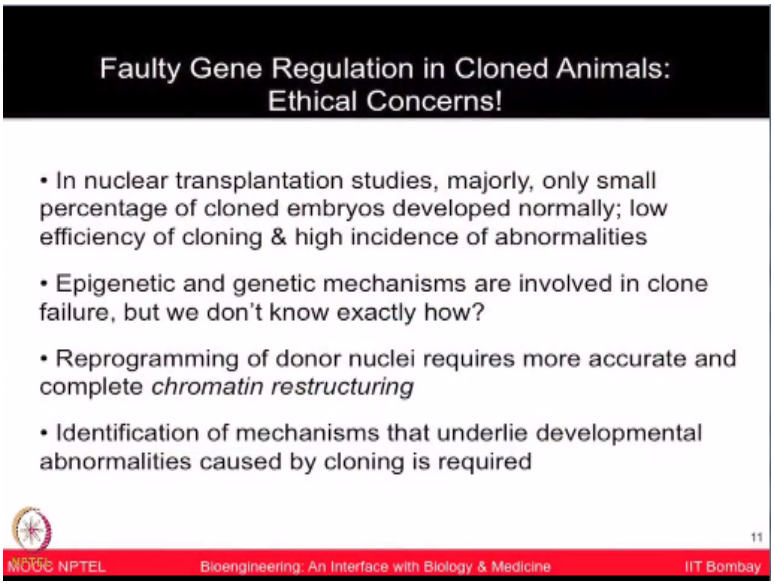

And then are you counting 20+6 years, so these are kind of questions there. So therefore you are not starting from 0 for again to reach that type of time life span so Dolly early death was one of the setback for the animal cloning field because then they cannot answer some of these kind of questions. And also many clones they encounter lot of abnormality.

So as I mentioned are their certain epigenetic factors many of the chromatin proteins which we talked little when we talked about histone protein and how they are involved in the chromatin modeling part. So some of those are the actually being involved for the reprogramming of the donor nuclei, and are they doing the chromatin restructuring which is equally important along with the genetic factors.

So some of these things have been the in the field a limitation a thought process against that you know why you should not use this particular technology at the mass production level. It has good proof of concept that now we have understood the cell biology and the developmental biology so well that we can do these things but it may not be require to attempt at that level.

So that particular you know, how to identify the mechanism which are underlying for these deficiencies or these kind of abrasions are very crucial. Before we do that we should not try to just attempt and keep making the clones which will be all kind of having variety of issue. So as a result people were actually you know the cloning for the animals were banned in US and the subsequently many part of the world and then only thing which people felt the need for it that can be used the cloning procedure for therapeutic purpose.

Can we take the cells which change the cells for the requirement of that you need at that time?

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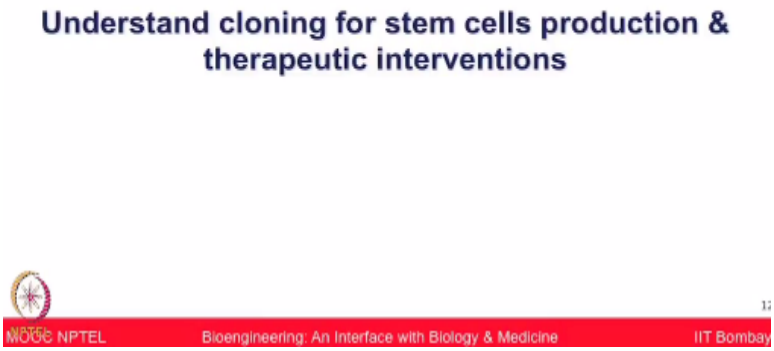

Let us say you need for you know somebody need for a heart failure that time or for a brain disorder. Can you take these cells embryonic stem and then you can transform into the right type of cell which you want to convert and use the cloning concepts for doing that at the cell level not at the full organism level? So understanding the cloning for the stem cells production was actually promoted and further continued for this field.

Stem cell you are going to study in much more detail in the you know, once I finish my part.

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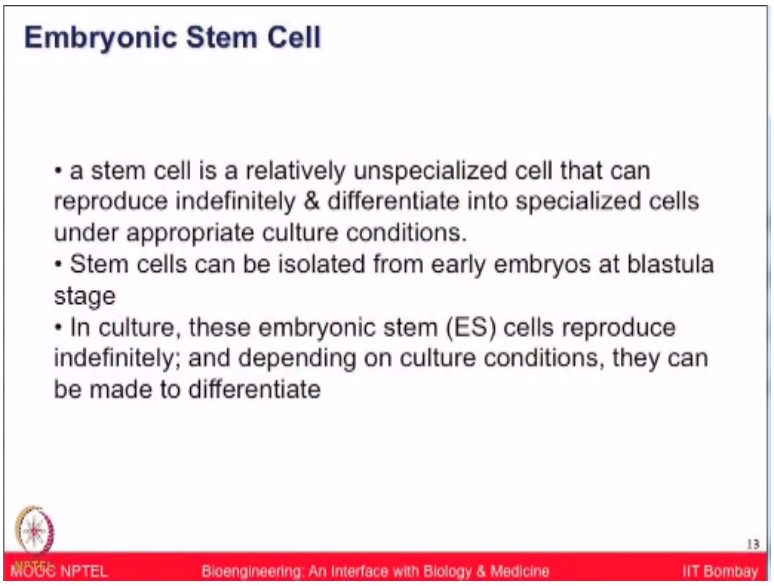

But in this context briefly, stem cells are those unspecialized cell which could be converted or modulated into a given specialized cell type if you provide them the right type of nutrients, right type growth factors at the very embryonic stage level. And you know it just shows that here that if you can culture this in different type of culture condition the same embryonic stem cell could be converted into liver cell or nerve cell or blood cell.

And I am sure you all understand and agree to it that these concepts has huge potential from the your medical point of view because one could use this for many deficiencies many diseases for replenishing the cells for the same individual because you know if you are taking the cell or different organ from somebody else then you will have always that you know the transparent issue, the rejection.

And then if you are growing the cell from the same individual and then you are transplanting back they will have much more advantages of taking it back.

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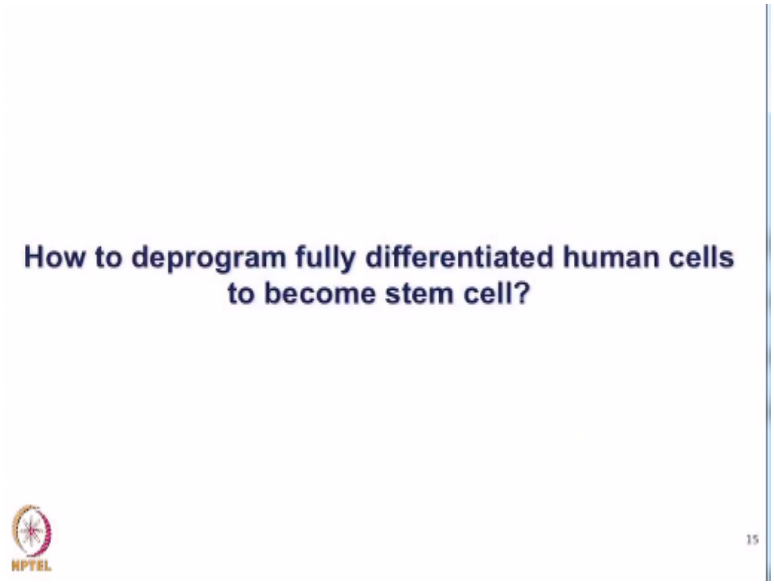

So how to you know, some scientists now plan an experiment that how to deprogram not reprogram but deprogram the fully differentiated human cells into the stem cell. So while one concept is you take stem cell, you are trying to convert those into you know specialized different type of cells. Can you take the differentiated cells? And now you are trying to make them as a stem cell. And this was one of the classical experiment not to the great extent I am going to talk.

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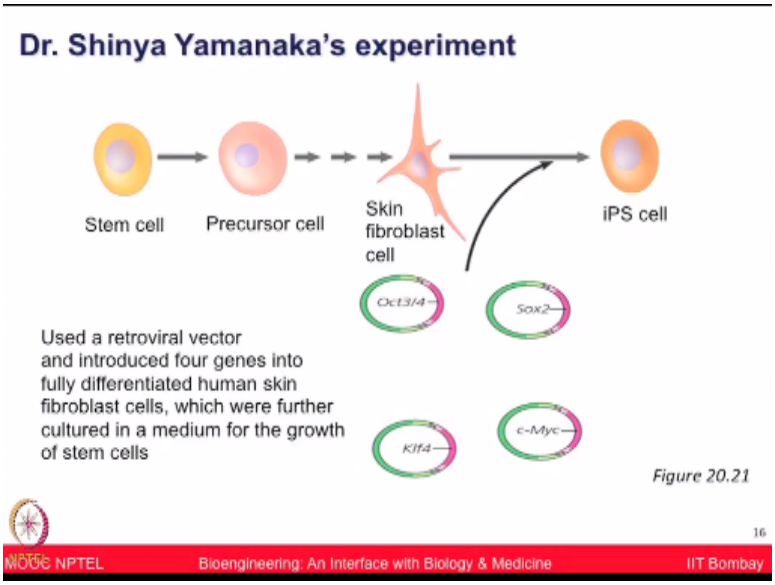

But just to brief you this one of the noble prize winning in research done by Dr. Yamanaka, Shinya Yamanaka in Japan. When they took some of the precursor cells, made this skin fibroblast and then actually they tried some transcription factors which are listed here which are Oct3/4, Sox2, Myc and Klf4. By addition of these transcription factors they were able to promote

generation of induced pluripotent cells, and that is kind of another experiment which led them to win the noble prize.

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So let me kind of take some time now and give you some perspective on how our understanding about this cell, cell cycle, cell reprogramming; how it has resulted into big scientific prizes and some of the scientific failovers and some of the scientific scandals.

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So now I talk to, you may not recognize them one of them is Sir John B. Gurdon which is shown here. He did the experiment of frog cloning which we talked in 1960s-1962 and Dr. Shinya Yamanaka in 2005 or 2006 he did the experiment of doing the cell reprogramming especially

stem cell experiment and both of them you know in some way looking at different type of cell reprogramming. They contributed to the basic research of how the cell can be reprogrammed.

And you know both of them made original contribution one at the level of the animal cloning level and one at the level of the stem cell and understanding about the induced pluripotent stem cells. So both of them were kind of you know basic research ground breaking research and both of them got noble prize for their contribution in 2012. (Video Start Time: 22:32)

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Next is the 2012 noble prizes. The first was awarded today for ground breaking work in reprogramming cells in the body as far as those achievements. The noble assembly at Karolinska Institute has today decided to award the Noble Prize in Physiology or Medicine 2012 jointly to John B. Gurdon and Shinya Yamanaka. The two scientists are from two different generations and celebrated today's announcement half a world apart.

But today they were celebrated together for their research led to a ground breaking understanding of how cells work. So John Gurdon of Cambridge University was awarded for his work in 1962. He was able to use specialized cells of frog like skin or intestinal cells to generate new tadpoles and show DNA could drive the formation of all cells in the body. 40 years later Dr. Yamanaka built on that and went further.

He was able to turn matured cells back into their earliest form as primitive cells. Those cells are in many ways they equivalent of embryonic stem cells because they have the potential to develop into specialized cells for heart, liver other organs. Dr. Yamanaka is currently working in Kyoto University. Embryonic stem cells had to be harvested from human embryos a source of debate and considerable controversy.

For Gurdon the prize has special meaning. At a news conference in London he recalled one school teacher reaction to his desire to study science. This is a completely ridiculous because there was no hope whatever of my doing science and anytime spent on it would be total waste of time on my part and part of the person having to teach him so that terminated my completely terminated my science in school. The man will receive their award in Stockholm in December.

Additionally, there are many scientists in the world who have been attempting to do the cloning experiments and many of them were successful as well.

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One of them shown here is Dr. Hwang Woo-Suk from Korea, South Korea. And he made series for cloned animals, one shown is, you know along with him is a dog but he made many cows which were all cloned. And you know in Korea people felt that you know he is going to bring lot of wealth lot of commercial value.

And probably you know so much income to the country because he has the capacity to do all this kind of cloning for their you know high yielding varieties which can give them good yield for different type of products. He became kind of one you know the big star in the field because he was doing series of these cloning experiment and showing one after other, they can clone many type of animals.

And then they were also you know attempting toward the stem cell research and sort some of their kind of experiment especially one of them is known as.

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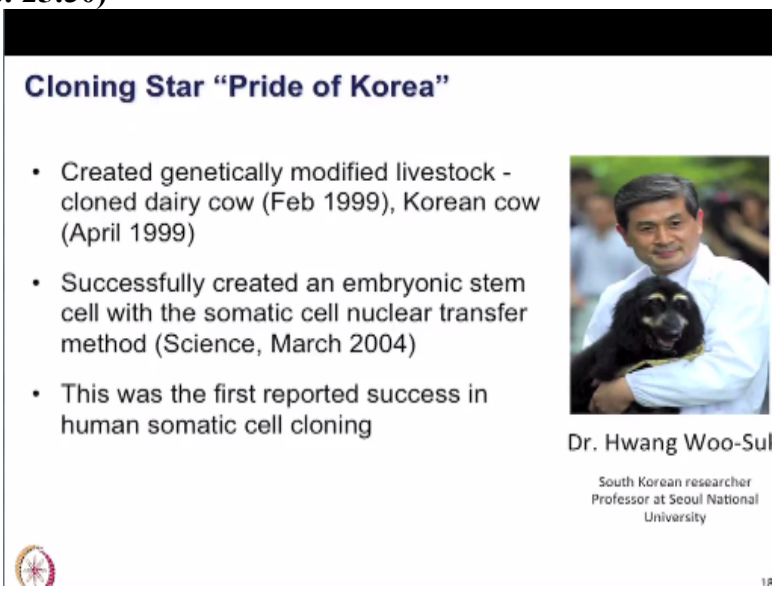

Somatic cell nuclear transfer which was published in one of the big general science. It is first time that, that has the potential to do the human stem cell cloning as well.

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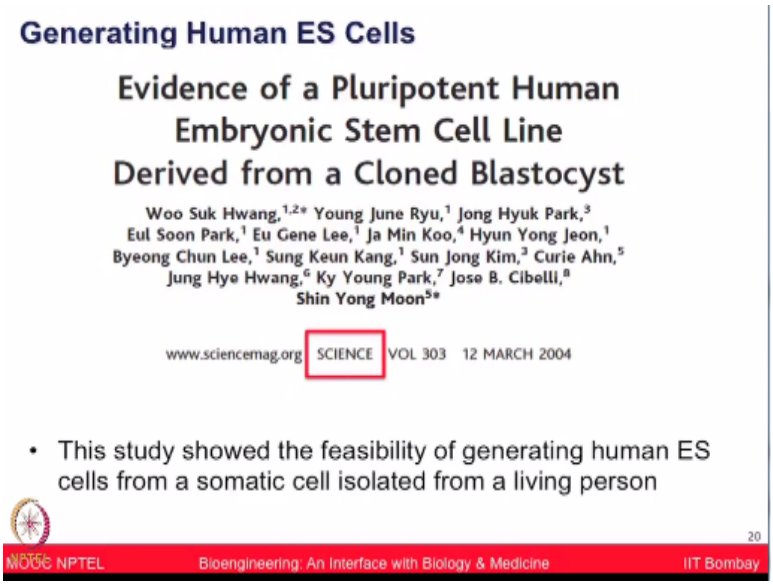

So after these research and they kind of published these words, if you are not aware in basic science field the general science and nature they are the top most journals which are highest in back factor generals. So you know you have lot of difficulty in publishing these journals until and unless you have a sound hypothesis and good experiment and validation done for those experiments.

So they did publish in science after Hwang Woo-Suk is the first author in this paper along with many of these authors when they showing that somatic cell nuclear transfer is possible to be done. They also showed another paper that they could now do the cloning of the blastocyst system which has potential for the human type of cloning human embryonic development and again published in science in 2004. So these two were kind of you know major breakthrough in the field and people are already finding him as a authority in the field.

So as a result you know many people started trying to replicate their experiment. And then after some time people roped to general science that you know there are some discrepancy which we find in these experiment we are not able to reproduce these results very well. I am sure you cannot read it from your distance here but some other things which I can read for you, so science general started investigation against this research and their work.

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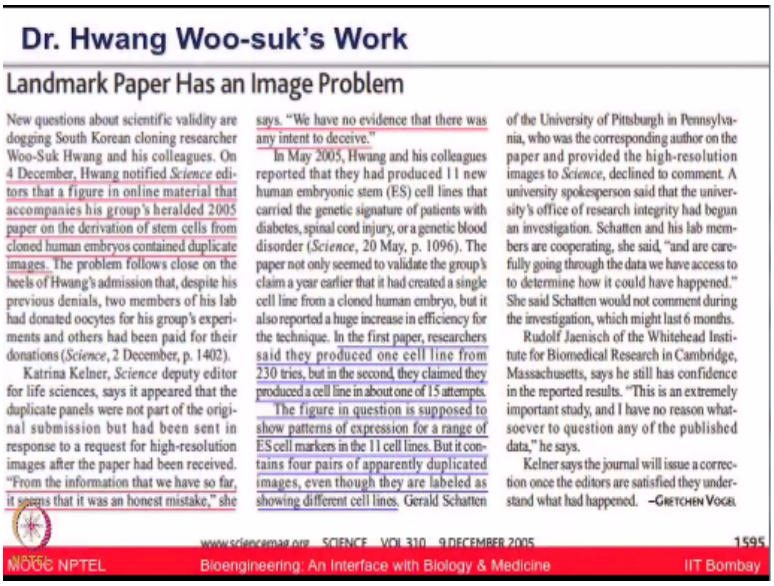

Dr. Hwang Woo-suk's Work

Landmark Paper Has an Image Problem

New questions about scientific validity are dogging South Korean cloning researcher Woo-Suk Hwang and his colleagues. On 4 December, Hwang notified *Science* editors that a figure in online material that accompanies his group's heralded 2005 paper on the derivation of stem cells from cloned human embryos contained duplicate images. The problem follows close on the heels of Hwang's admission that, despite his previous denials, two members of his lab had donated oocytes for his group's experiments and others had been paid for their donations (*Science*, 2 December, p. 1402).

Katrina Kelner, *Science* deputy editor for life sciences, says it appeared that the duplicate panels were not part of the original submission but had been sent in response to a request for high-resolution images after the paper had been received. "From the information that we have so far, it seems that it was an honest mistake," she says. "We have no evidence that there was any intent to deceive."

In May 2005, Hwang and his colleagues reported that they had produced 11 new human embryonic stem (ES) cell lines that carried the genetic signature of patients with diabetes, spinal cord injury, or a genetic blood disorder (*Science*, 20 May, p. 1096). The paper not only seemed to validate the group's claim a year earlier that it had created a single cell line from a cloned human embryo, but it also reported a huge increase in efficiency for the technique. In the first paper, researchers said they produced one cell line from 230 tries, but in the second, they claimed they produced a cell line in about one of 15 attempts.

The figure in question is supposed to show patterns of expression for a range of ES cell markers in the 11 cell lines. But it contains four pairs of apparently duplicated images, even though they are labeled as showing different cell lines. Gerald Schatten of the University of Pittsburgh in Pennsylvania, who was the corresponding author on the paper and provided the high-resolution images to *Science*, declined to comment. A university spokesperson said that the university's office of research integrity had begun an investigation. Schatten and his lab members are cooperating, she said, "and are carefully going through the data we have access to to determine how it could have happened." She said Schatten would not comment during the investigation, which might last 6 months.

Rudolf Jaenisch of the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, says he still has confidence in the reported results. "This is an extremely important study, and I have no reason whatsoever to question any of the published data," he says.

Kelner says the journal will issue a correction once the editors are satisfied they understand what had happened. –GRETCHEN VOGEL

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And they mentioned from the information that we have so far it seems that they have made some honest mistakes, we have no evidence that there was an intent disease but they still kept their research on hold and then they you know started investigating more. But many people observed that many of the claim what they have done in the papers are actually not meeting to the right experimental requirements and others are not able to reproduce those experiments.

So after sometime their university started investigation and then they found series of allegations and series of issues which were involved in this experiment. And as a result, you can see this news clip here. (Video Start Time: 27:38)

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The great stem cell researcher Hwang Woo-Suk has been sentenced to 1 year and 6 month prison and 2 years of probation for embezzling state and private funds and buying human eggs. (Video Start Time: 27:47)

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The Supreme Court issued the verdict Thursday which comes 8 years after he admitted to faking his research. The outstate zone National University professor was in guided in 2006 on charges of fabricating the results of his human stem cell research and embezzling nearly 2 million US dollars in research funds from the government and two domestic companies SK group and NongHyup. (Video End Time: 28:11)

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Well, so there was you know rise and fall of this chart; lot of things happened from 2004 onwards. He was sentenced to jail he again try to come back again tried attempted some experiment, but once people you know lose trust you lose confident on you it is very difficult to make comeback, so he did try to show some successful experiment afterward but then there is no authority to accept those results.

Another story developed with Dr. Haruko Obakata from Japan and she was trying to, she was Japanese scientist like Dr. Yamanaka and she was trying to see that you know can she work on stem cell part and make the process of cell reprogramming much similar.

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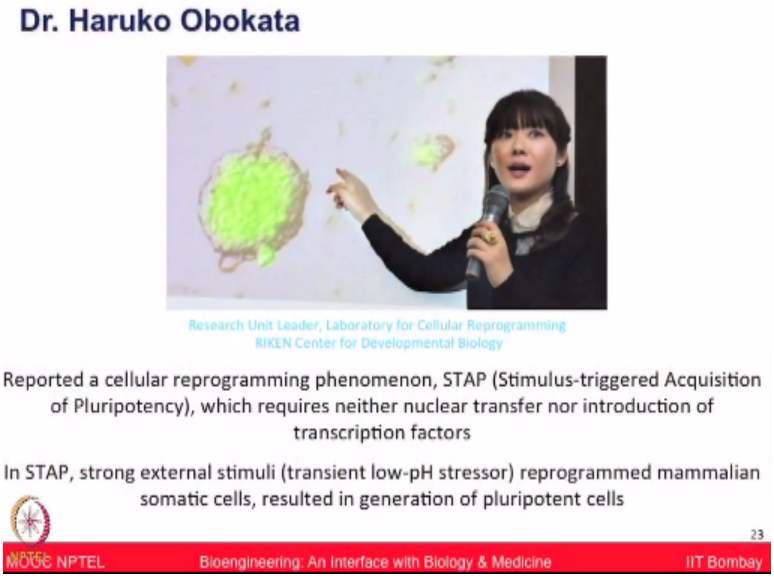

And she came up with the concept which is known as STAP or Stimulus-triggered Acquisition of Pluripotency where she said that you know rather than using those genes or transcription factor which Dr. Yamanaka showed for the noble prize winning study, you know you can just simply change the pH of the medium and just that pH triggered itself could actually lead to those gene changes which could acquire the pluripotency.

And that was something you know which brought very noble kind of concept. And she published this work in another distinguish general which is natured.

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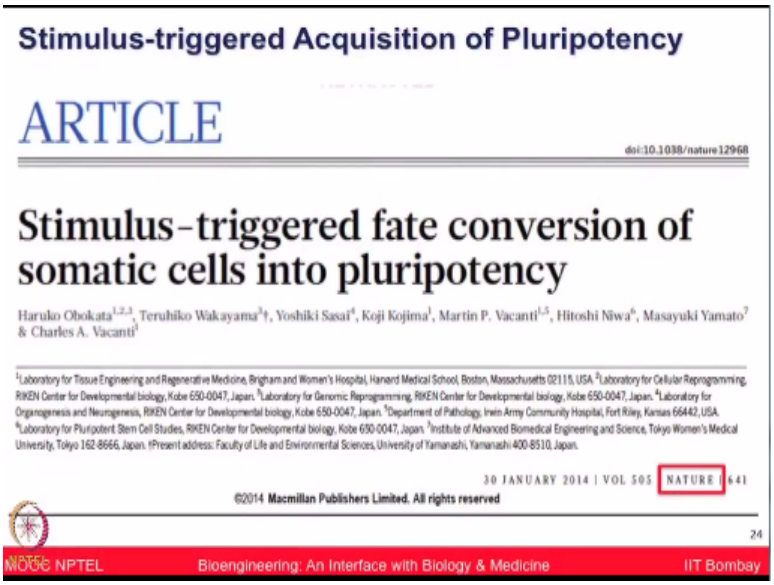

Which you can see here and she is the first author of Stimulus-triggered fate conversion of the somatic cell into pluripotency.

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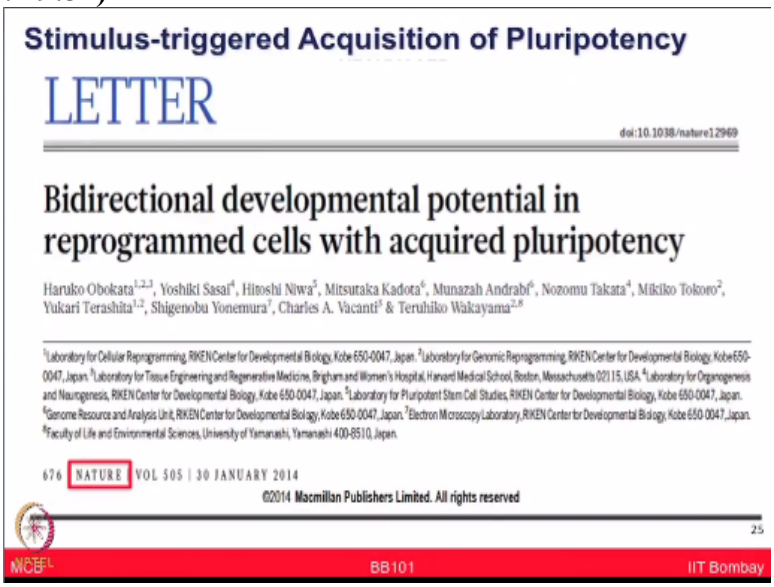

Another paper, they also published again on the same concept in 2014; these are much more recent studies. Then people started following up you know how simple this thing can be now and can be reproduced those. And when they started reading their papers much more in detail they found that there are lot of issues in the images or in this particular paper.

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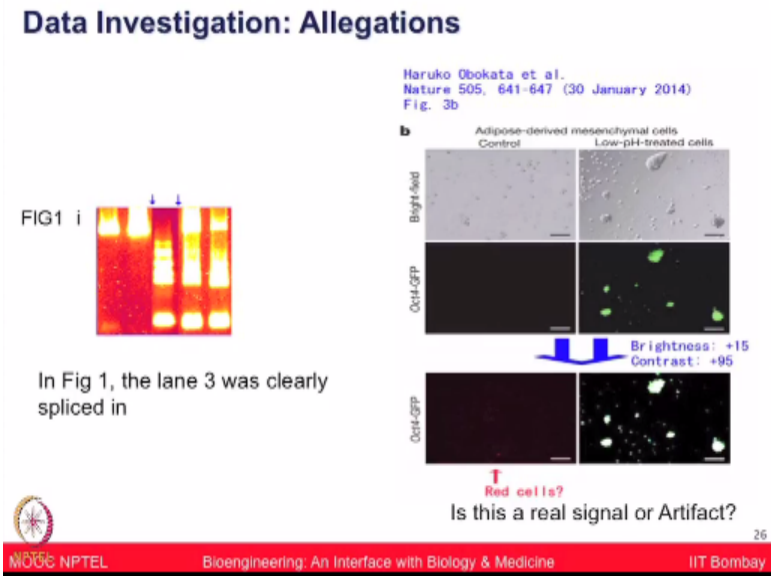

This lane looks like something has been taken from some other gel and brought it and put it here which is not belonging to this experiment; they are looking at the DNA profile here. In this field they are looking at the cell under microscope and just by changing the contras or brightness probably you can make something looks like whites stinge which is not actually accurate.

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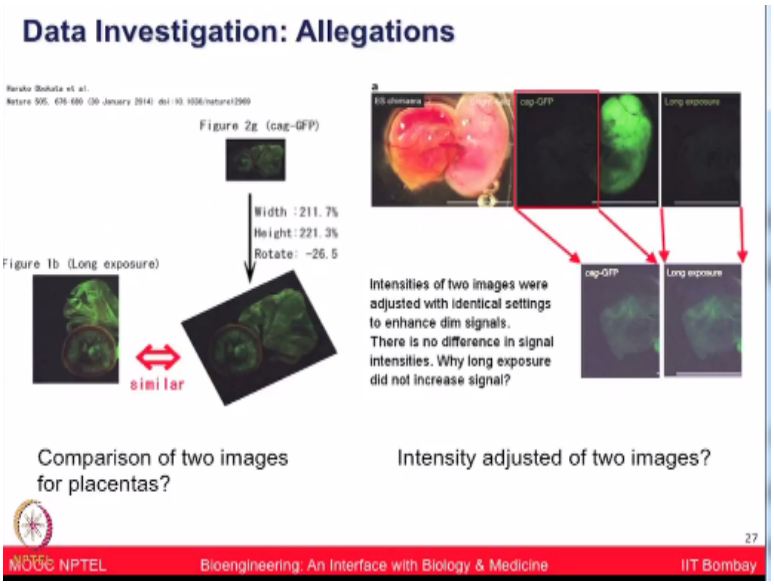

Or by inventing the, you know embryo part of the images you are making it look like this, so many of these observations are made. People started investing against these that many of these things are not actually represented, looks like has been played quite a bit of the image processing site and they are not the accurate reflection of what result one could obtain. So, with all of these issues when now their university started investigation again toward them and it is much more

serious investigation; much more recent thing and let us listen what happened here. (Video Start Time: 30:46)

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Scientist from a leading Japanese researcher have apologized for the grave mistakes in recent papers on a new way of creating stem cells. The research was hailed as a revolution discovery when published in January in the British General Nature about but doubting questions about the methodology and results forced the decant centre to take action. NHK World, TaKafumi Terui, Ereport. Decant scientist spent about 4 hours in the front of the cameras talking about what has become an international scientific scandal.

They say the findings of their investigation into the stem cell studying question was still inconclusive. They know that they have seen no evidence of deliberate data manipulation so far. But the presence of (()) (31:37) who is a noble of the chemistry acknowledged serious mistakes were made. I would like to first and foremost express my deepest regrets that article published in nature by our scientist bringing into question, the credibility of the scientific community. (Video End Time: 32:08)

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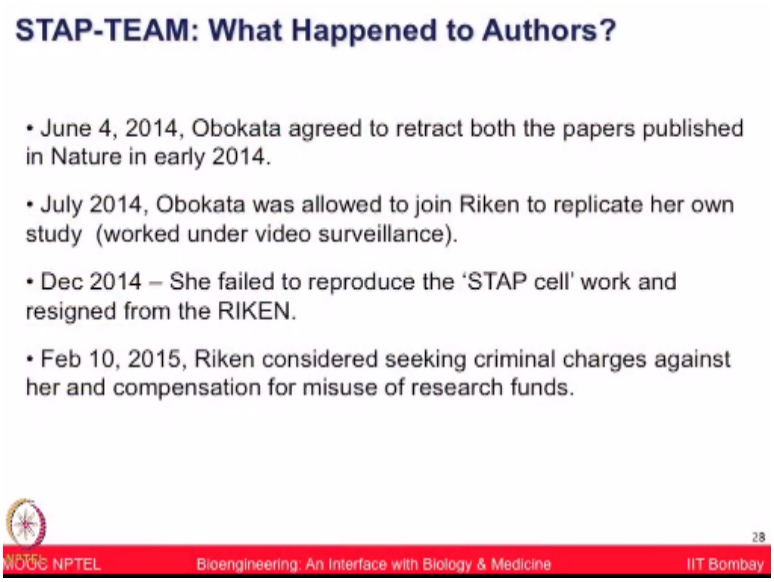

All right, well so you know when you are a part of ambitious project sometime you are competing for you know something to make device, something to make product something to compete for international competition, you are part of a team and that team is actually trying to compete you are best in the world, right. In the process, you know sometimes you just get to greedy and then you start thinking about some fined tuning and that could lead towards some sort

of fraudulence as well, exactly what happened in these cases. And if you are part of those team you are equally involved. Even if you are not the one who has committed the mistake you will be still considered part of that team and you are you have to own that particular problem yourself. So in this case every author even those who have not committed the mistake even all those authors they actually where punished. They were all removed from their jobs, their salaries were taken some of them were sent to jail.

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This is, you know a nature general route what the punishment were there for all the scientists involved in the STAP research. So every scientist actually you know who are involved in the paper even they may not be in aware that something like this fraudulence happened. It is your responsibility as a part of that team you to ensure that you are also confident about that work and that research that is happening. So it is very crucial to just get the you know, when you are trying to get the glory you have to also own the failures of that team.

So but what was the most you know disheartening to see one of the researcher committed suicide after this particular failures and this particular retractions in the same lab they committed suicide and this was very you know sad to see the fate of full team and what has happened to that. So if I just kind of summarize this part, although we are talking about cell reprogramming.

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But it is always something to learn and those lessons could be much bigger than just learning development. So cell reprogramming, we talked about some of the basic fundamental research which gave into the noble prizes. We also seen that some of the fall of stars which try to reach to the same level but use some sort of fraudulent ways of reaching their and that was not so appropriate.

So it just brings you know I think last two minutes I will take to summarize that, you need to follow some ethics in research and publication especially in the kind of profession we all work whether you are engineers or somebody biologist or medical practitioner, society have lot of expectations from us and they do believe that whatever we report is actually very accurate. So I think your devices, your models your analysis has to have their own values those meaning and then only I think you know people are going to have trust in us.

And as I mentioned many times you know you are all going to compete for many other competition in the world. Please ensure that you are following the ethics in whatever work you do and that is very crucial not only to study development but also for your day-to-day kind of life achievements. So in today's lecture, we tried to understand some of the phenomenal involve in this cell reprogramming. Many elegant experiments done for the cloning especially different type of animal were cloned.

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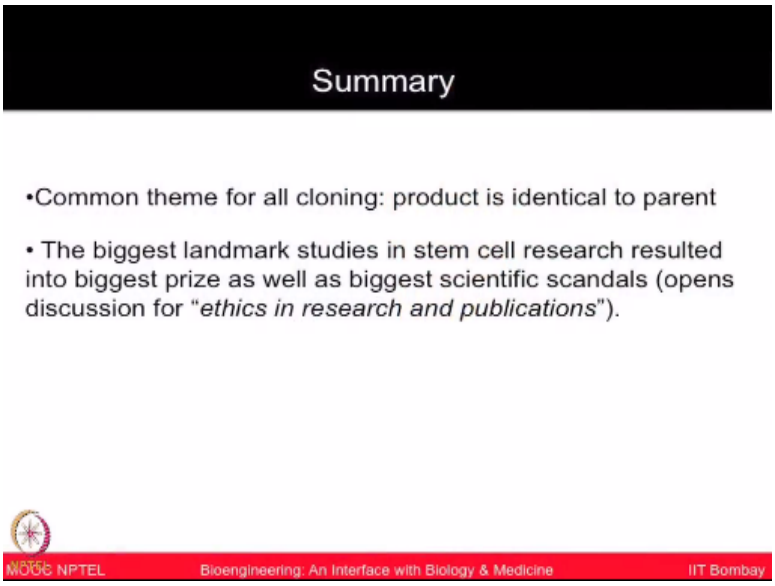

And later on stem cell cloning was also performed. With did not try to take a case study and interesting story to see that how different experiments or the major breakthrough which were reported in the studies; some were based on the sound understanding related into the noble prize. Some of them were also fraudulent research and were actually penalized and became one of the scientific scandals of the field.

Other important to understand that this concept of cloning is you know is on one hand it is like a scientific fiction for us which looks like getting true; at a same time have many ethical issues involved because when to clone; why to clone and what impact it may have for the society. At a same time from the case study you would have witnessed that you know what practices that should follow in doing the scientific experiment is very crucial.

So let us continue some of these discussions about the science ethics involved in doing these kinds of experiment and what to be reported in research and publications. Let us continue that in the next lecture. Thank you.