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# Episode 4: Stem Cell Research

## Stem Cell Research

VOICEOVER
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JACKY
Welcome to Melbourne University Up Close. I!|m Jacky Angus at the Melbourne Research Office. In today!|s Podcast, we consider the topic issue of therapeutic cloning, that is cloning of human cells for therapeutic purposes. This process which involves somatic cell [nuclear] transfer, SCNT enables scientists to develop cell lines for research into a range of illnesses such as Motor Neurone Disease, Parkinson!|s, Diabetes, and Alzheimer!|s. One of issues this raises is whether it is acceptable to create a process that produces life simply for the purpose of research. To better inform Australians on the debate, an enquiry was established last year, headed by former judge John Lockhart. The Lockhart Review addressed the sorts of questions being asked in the wider community about Embryo[nic] Stem Cell Research, and if permitted, how it should be regulated. What are the implications of allowing scientists greater freedom in research? Is it justified, or is it going too far? Can such research be controlled to avoid exploitation, for example, the commercialisation of human eggs? On the other hand, if at least a solution that dramatically improves the life of people with degenerative diseases, is it right to prevent this. To address these important questions, I have two guests with me in the studio today, both of whom are ideally placed to help unravel this very complex subject. They are Professor Loane Skene, an expert in health law and human ethics at the University of Melbourne. As deputy chair of the Lockhart review, Professor Skene also appeared before a senate community affairs committee. My other guest is Professor Peter Rathjen, Dean of Science here at the University of Melbourne. As an expert on cell specialisation and differentiation, Professor Rathjen will help clarify the scientific issues involved. Good morning and welcome to you both.

PROFESSOR RATHJEN
Good morning.

PROFESSOR SKENE
Thank you Jacky.

JACKY
Professor Skene if I can start with you, so far in Australia the government has passed two acts, the research involving human embryos act and the prohibition of human cloning act. So what!|s changed since then? Why do we need newer legislation?

PROFESSOR SKENE
Since then there have been a number of scientific developments which Professor Rathjen could explain more fully than I will, and also changes in community attitudes. When the legislation was passed, one of the provisions in the act was that there should be a review of both of those things, developments in science and changes in community attitudes. And that this committee should report to the parliament and in the light of that report, the parliament may decide that it should change the legislation to allow, particularly, somatic cell nuclear transfer.

JACKY
Well, as Deputy Chair of the Lockhart Review, what were your recommendations.

PROFESSOR SKENE
The first recommendation was that the committee supports the current national legislation. And this makes it a crime to do certain things. For example, it!|s a crime to create an embryo and implant it with the view to cloning another person. We call that reproductive cloning and that!|s !V should remain prohibited. It is also a crime to sell human sperm eggs and embryos. And it!|s a crime to create or try to create human animal hybrids. And we said that all of those should remain crimes to allay any community concern that scientists might try to do these things. Secondly we said that the current embryo research should be permitted to continue and at the moment scientists are permitted provided they get a licence, to do research on excess embryos that have formed for use in fertility programs that are needed by the !V the couple because they!|ve already finished having their family or they decide not to proceed with it. If those embryos are not used in research or donated to another couple, they have to be destroyed under the legislation. Thirdly we said that the current licensing system should continue because it provides an open transparent system of ensuring that every application to use an embryo in research is overseen by a licensing committee and a report is made which becomes public. But we also said that other research is needed with regard to embryos and also to improve fertilisation procedures in reproductive technology programs. Finally we recommended that somatic cell nuclear transfer should be permitted. This would enable matched cells to be developed that would be compatible with the person whose body cell is used to create the human embryo. This is contentious because people say that it!|s creating a human embryo with a view to destroying it. However this type of embryo was regarded by the Lockhart Committee as being quite different from an embryo that!|s formed by a couple trying to have a baby from their own

sperm and eggs. The somatic cell nuclear transfer process is more like growing your own cells for the purposes of a skin graft for example. It!|s more like treating yourself by the process rather than trying to form a baby.

JACKY
One of the questions I suppose that some people might ask is who decides these things, who!|s on the committee for example that you know you were involved in? Is it just scientists and politicians?

PROFESSOR SKENE
One of the interesting things about the Lockhart committee was that it drew heavily on the University community. It was chaired by a retired federal court judge, Justice John Lockhart, who sadly and very suddenly died just after the report was completed. But the other members of the committee were all in universities. They brought their academic expertise to the conduct of this enquiry.

JACKY
To what extent do they represent people in the wider community. I!|m thinking of you know, the average mum, perhaps, or people that go to church, and people that are interested but really don!|t know much about this whole business.

PROFESSOR SKENE
We did undertake very thorough consultation during the work of the committee and in particular we had over 1,000 written submissions, we had public hearings in all of the capital cities of the states and territories, and we also interviewed many of the stakeholders. But the other thing is that people are members of more than one community and although you might say here are the scientists, and the !V it!|s the religious people that are against them, in fact of our number there were a number of people who are practising Christians, in fact four out of the five, so !V

JACKY
That!|s interesting.

PROFESSOR SKENE
!K and we!|re church goers, and we !V of course we!|re family members, and we have relatives who !V who have genetic conditions, so although we!|re academics, we!|re also members of these others communities that might have views on these issues.

JACKY
You!|re listening to Melbourne University Up Close. I!|m Jacky Angus and I!|m speaking to Professor Loane Skene and Professor Peter Rathjen on stem cell research. Well now, can we look still, Professor Skene, if I may, before we turn to the science, can we just consider the question of exploitation and commercialisation. I know some people are concerned that for example women will be pressured to produce and provide eggs for this process.

PROFESSOR SKENE

This is one of the things that many of the feminist groups have been concerned about. Certainly in the early stages it will be necessary to be asking women to donate their eggs. The women who!|ll be asked to donate are women who are in fertility programs and they!|re already having the eggs collected for the purposes of assisted reproductive technology. These eggs will be used in research principally and although some people have said what about when we!|re doing all of the research in the future, for people who have diabetes for example and there!|ll be !V there will be hundreds of thousands of people, I think it!|ll be possible to get eggs from other sources, one source from the embryonic stem cell lines themselves. So what we!|re looking for at the beginning is not a huge number of eggs, but the other point is that the Lockhart Committee recommended that only for research, it should be permissible to take rabbit eggs, and of course, rabbits breed like rabbits, and take the nucleus out of the rabbit egg, put the nucleus form the !V the human donor if you like into that rabbit egg and grow the embryonic stem cell lines. Now this would obviously mean that the stem cell lines would be available for research and it wouldn!|t be necessary to use so many human eggs. There is a yuck response, people don!|t like the idea of this, but you!|ve got to emphasise that it!|s being done solely for research and the entity that it would be created in this way, would not be allowed to be implanted into a woman or into an animal and anybody who tried to do that, even if it were possible, would face the prospect of 15 years in prison.

JACKY
Well that!|s a relief, I must say. Given the scientific change is constant, does that mean that we need to look at this legislation again in two or three years. Is there any consideration of that given by the Lockhart Review?

PROFESSOR SKENE
The Lockhart Review recommended that there should be another review of the Act in three years time and if the Lockhart Committee!|s recommendations are adopted, that!|s likely to be the case.

JACKY
If I can now turn to Professor Peter Rathjen to clarify some of this complex stuff in scientific terms, can I start by asking you what the difference is between stem cells from the adult and embryonic stem cells.

PROFESSOR RATHJEN
If you think about how we started life, it!|s a nine month process in a human, and we started a life as a single cell which was a fertilised egg and from that cell remarkable things happened over nine months. The first thing that happened was there was an increase in cell number, so that we finished up with several trillion cells in our cells at birth, never several hundred thousand, never lots more cells, it!|s carefully controlled. We started life as a single kind of cell which was a fertilised egg but by the time we!|re born we have several hundred different kinds of specialised cells in our bodies. They carry oxygen if they!|re haemoglobin positive or red blood cells, they are hair cells, they!|re muscle cells and skin cells and so on. And that gave us the right kinds of cells to make up a specialised organism like ourselves. Those two

processes gave us the right number and the right kind of cells. The third process that was at work was to organise those cells into a structure that looked like a human. Now if you look at embryogenesis it!|s starting at the fertilised egg cell stage, that is all correct, but equally, you can look at embryogenesis as starting a little later in a structure called the blastocyst. And in the blastocyst there!|s a particular group of cells, a small number of cells, some tens of cells which we call the inner cell mass. As best we can tell, those cells are the same and any one of them can take the journey that I!|ve just described. It can turn into those trillions of cells. It has a property which we call pluripotence, which means it can turn into any other kind of specialised cell, a process we call differentiation.

JACKY
This is in the embryo, we!|re talking -

PROFESSOR RATHJEN
This is in the embryo. Those cells, the inner cell mass cells are the true founder of all of us and we call them the stem cells. When we work with them and isolate them in a laboratory they are devoid from the other embryonic tissues and we then call them embryonic stem cells. But embryonic stem cells therefore are a normal population of cells that are found at the earliest stages of our gestation and whose normal role it is to turn into the cells that make up our bodies.

JACKY
So they!|ll turn into adult cells eventually?

PROFESSOR RATHJEN
They will turn into adult cells that is correct, in fact they will turn into all adult cells. Adult stem cells are rather more elusive. We know there are some poorly described cells that sit in particular body compartments, for example the bone marrow is one, and the brain is another. We know there are cells in there that can differentiate into other cell types, but it is fair to say that at this stage we are not good at identifying those cells, we are not terribly good at growing those cells in the laboratory and we don!|t know very much about what sorts of cells they can differentiate into.

JACKY
What would you grow them into if you could?

PROFESSOR RATHJEN
Well what would be rather attractive is if you could take a bone marrow biopsy for example, grow up the stem cells from that bone marrow and then be able to differentiate them into blood cells if you want to replace blood, but perhaps nervous cells if you want to reseed some structures in the brain or heart cells if you wanted to reform the heart. We !V

JACKY
So if an adult had - had some sort of disease, one would hope that you could use those cells to regenerate their own tissue, is that what you!|re saying?

PROFESSOR RATHJEN
That ideally is what adult stem cell researchers would like to accomplish. But as I say it is difficult to identify and to grow the cells and we simply don!|t know enough about what they normally differentiate into. One thing we do know is that for example a cell in the bone marrow does not normally differentiate into a nerve cell, whereas, of course, the contrary is true of an embryonic stem cell which absolutely does do that as a normal part of embryonic genesis.

JACKY So you do use adult stem cells, but they!|re not necessarily as useful to research as embryonic stem cells, so to speak?

PROFESSOR RATHJEN And that would be because our lack of knowledge about how to grow them and because we don!|t know how to turn them into every other kind of cell. Those may be scientific problems that could be solved going forward into the future, and that is what adult stem cell biologists are trying to do, but at this stage it would be premature to say that we can do either of those key steps.

JACKY So therefore, the objection to this legislation is really based on medical grounds as well, that, you know, it!|s more practical to start looking at embryonic cells because they actually can do the work. Is that what you!|re saying?

PROFESSOR RATHJEN I think that is a perfectly reasonable philosophical argument, yes.

JACKY So can we now then turn to embryonic stem cell research, why is that so important at the moment?

PROFESSOR RATHJEN I think there are really three different lines of investigations that people are interested in, and the one that!|s received the most media attention is the possibility of generating cell populations that we could transplant to try and cure diseases that are caused by the dysfunction or the loss or the damage of unique cell populations within the body, so that you might be able to cure immune deficiency for example by generating immune system cells and transplanting them back into people with that disease, or perhaps treat Parkinson!|s Disease by making cells that are equivalent to the nerve cells that are lost in Parkinson!|s and transplanting them back into the brain so that you might be able to restore normal function to Parkinsonian sufferers. There are a large number of diseases that are caused by dysfunctional cells in our bodies. They tend to be increasing in prevalence in western societies because they are associated with aged populations. They tend to be the sorts of diseases that are associated with quality of life rather than quantity of life, and so the idea is that with the embryonic stem cells themselves, we may be able to grow them to large numbers as a stem cell and then to control their differentiation to the target cell population that would need to be transplanted to restore function in a sick human.

JACKY
That!|s certainly very impressive. Of course one of the problems is that people object

to the idea of growing these cells because they see them as representing human beings, at least human potential. How do scientists deal with that? I mean, science just doesn!|t generally have a time when you can say that the human life exists, is it right? It!|s fairly flexible. Is that right?

PROFESSOR RATHJEN
There are two lines of argument there. The first is there is not good consensus amongst the scientific community about when life begins within the embryo. There is, I believe, very strong consensus within the scientific community that an embryonic stem cell, a human embryonic stem cell cannot be considered to be alive or to have the potential for life. There is not an obvious environment that you could put it into where it would give rise to an organism.

JACKY
So it would die anyway if you didn!|t implant it?

PROFESSOR RATHJEN
It would !V it needs to be kept alive within the laboratory. It is not an embryo, and it does not have the capacity for organization that would be required to create an embryo. I said initially that you need the right number of cells and the right kind of cells and the organization of those cells to get an embryo and then an adult. An embryonic stem cell has no capacity to organise itself in the way that would be required. I commented that there were other ways in which embryonic stem cell research was likely to be important. The second way is simply in terms of our understanding of the normal human and the diseased human. By taking embryonic stem cells and studying how they form normal tissues, we will learn a great deal about how the human comes into being. But secondly by taking embryonic stem cells with the mutations that underpin human disease we can potentially start to decipher what goes wrong as you form aberrant cell types in certain kinds of human disease, particularly as it pertains to their development ontogeny. And the last thing that many of us are excited about is increasingly it is becoming apparent that the body itself has significant regenerative activity that when you damage an organ the body tries to replace the cells that have been lost and for various reasons it!|s not terribly efficient at that. One of the ways that we might be able to treat these diseases is to understand the molecules or the drugs that could be used to assist that process in individuals that have disease. To discover those molecules we!|re going to need cells that enable us to discover their identity and how they work and we have good reason to believe that embryonic stem cells may be a very useful cell population to help us discover drugs that we could then go on and use in the way that I!|m talking about.

JACKY
Well there are controversies associated with the growth of these cells, these embryonic stem cells aren!|t there?

PROFESSOR RATHJEN
No in fact I believe that!|s not the case. The growth of the cells is not controversial, they grow very similarly to other cells that we!|ve been growing in the laboratory for

many decades. There is controversy about the methodologies that are currently used to isolate those stem cells from the embryo in the first place and the reason for that is that the isolation of embryonic stem cells from an embryo requires destruction of the embryo at that stage. Once they have been isolated they are immortal, they can be transported around the world, and grown and studied in different laboratories and the actual growth of the cells, the proliferation of the cells I believe has no significant opponents.

JACKY
But in the wider world, I suppose in the !V in the general non-scientific community there is real concern about the destruction of embryos, isn!|t there, particularly amongst the religious community.

PROFESSOR RATHJEN
The debate is that an embryo was created by SCNT and then destroyed to give rise to an embryonic stem cell line. Opponents of this technology say that the embryo itself was alive and that therefore we have given rise to this life in order to destroy it. Now the argument that!|s !V it is alive, is largely based on its potential to give rise to a viable human being and that potential requires for it to be put into the right environment which is the womb. And we know that if that is done, then with low frequency, you could get a cloned human. I say low frequency because the technology that was used to give rise to Dolly the sheep worked very badly and there were some 250 attempts before they were successful once. But one of the arguments that!|s been brought to my attention more recently is if legislation prevents you from returning that embryo to the womb !V

JACKY
As it does.

PROFESSOR RATHJEN
As it does, and if you!|ve created that embryo without any intent of ever doing that in the first place, then did that embryo in fact ever have the potential to give rise to life? And I believe that was tackled as part of the Lockhart Committee!|s deliberations.

PROFESSOR SKENE
Yes we took the view that the somcatic cell nuclear transfer embryo is different in its moral status from an embryo formed by a couple with a view to it being transplanted. That!|s made from their gametes and the purpose of it is to have a baby. With the somcatic cell nuclear transfer embryo it!|s produced with a view to producing embryonic stem cells currently for use only in research if it were allowed, but in future perhaps be also for therapeutic uses. But it!|s never intended that this should be implanted and in fact that would be prohibited by the legislation.

JACKY
Some scientists do consider that we!|re over-optimistic about what can be found from embryo stem cell research? Isn!|t that so?

PROFESSOR RATHJEN

There is a small group of scientists that believe there might be some barriers to implementing the technology. That is pretty standard for any kind of new scientific advance. Science proceeds incrementally towards an end goal, and there have been a number of independent reports just recently to have a look at how embryonic stem cell research has proceeded in about the last 8 years since the cells were first reported. And I think without exception they come back with the advice that the progress has been spectacular, it!|s been in many different fronts. Human embryonic stem cells have not yet been used to treat diseases in humans. They!|ve actually been used to cure diseases in animal models, but that!|s not quite the same thing. It!|s a !V it!|s a precursor step to identifying human therapies.

JACKY
What has been achieved so far?

PROFESSOR RATHJEN
You need to understand that until recently only a very small number of laboratories in the world could grow human embryonic stem cells and most of them could not grow those cells very well. They were not pure, they were not stable. Recently we!|ve been able to develop new culture conditions which means we!|ve eliminated what was previously a requirement for animal cells and animal products to be cultured with the cells. That means we have new lines of human embryonic stem cells that are likely to be approved for transplantation into humans. They did not exist five or six years ago. We!|ve learnt a great deal about how to control the differentiation of those embryonic stem cells into something that might be transplantable. Nerve cells for example or heart muscle cells. And to our great satisfaction the pioneering work that!|s been carried out in mouse embryonic stem cells generally turns out to be applicable to human embryonic stem cells.

JACKY
With what diseases?

PROFESSOR RATHJEN
I'm sorry, this is just forming the cell types in the first place. But then, people have gone ahead and more recently using human embryonic stem cells, started to generate cell types and transplant them back into rodents to treat rodent models of disease. And there we are talking about diseases like Parkinson!|s Disease or spinal chord injury or animal models for diabetes for example or animal models for immune system dysfunction. It seems almost that each week you pick up the journals, and there is another report of a stem cell that!|s been used to treat a disease. One of the things which is about to happen is that they are starting to plan and enrol patients for the first human clinical trials which will be carried out in America, I understand in 2007. So we!|re starting to see the normal scientific progress from the Petri dish to the patient and the final things that I think!|s been very important is that we!|ve gone from a very small number of researchers who could grow these cells badly a few years ago to now a very large number of laboratories that can grow these cells well in 2006. These are spectacular advances. Critics are right to point out that no disease has yet been treated. That is correct and that will be correct right up until we

do the clinical trials and test whether in fact the technologies can work.

JACKY
You!|re listening to Melbourne University Up Close, I!|m Jacky Angus and I!|m speaking to Professor Loane Skene and Professor Peter Rathjen on stem cell research. Can I give the last word to you as the scientist, Professor Peter Rathjen? Do you think that in the future people will be better informed about scientific procedures? It seems that slowly this kind of information is getting out to communities.

PROFESSOR RATHJEN
We have a particular problem with biological advance, the next 50 or 100 years will be dominated by the applications of biotechnology but generally speaking our population is not well educated in the unbelievably rapid advances that have underpinned biology. As scientists we simply have to take it upon ourselves to get out into the schools, out into the community groups and into the population generally and continue to educate them so that they can have scientifically informed decisions about where their future might lie. It is I think important to get across the concept that this is a global activity and so there are two things about that. One is wherever the cures are developed the patients will flock to avail themselves, whether it!|s in Australia or not. The second is of course that we!|re in a global scientific race to create industries and value for our countries and Australia is but a small player.

JACKY
We do seem to be a pretty er significant player however don!|t we?

PROFESSOR SKENE
We!|ve been a significant player in reproductive technology research from the start and at the University of Melbourne we have one of the great biomedical centres in the world. If our scientists are not able to do this sort of research in Melbourne they will go somewhere else. And the type of research that we!|re talking about involving somcatic cell nuclear transfer is lawful in the UK, it!|s lawful in a number of Asian countries and it!|s lawful in America in many states, provided that you don!|t use federal funding for it. So our scientists will certainly be able to find other places to go, the research will be done. I think eventually cures will be discovered and Australia will miss out on the financial returns of them.

JACKY
Well let!|s stay optimistic. Thank you both for joining Up Close today. Professor Loane Skene and Professor Peter Rathjen. Thank you both.

PROFESSOR SKENE
Thank you.

JACKY Melbourne University Up Close is brought to you by the Marketing and Communications Division in association with Asia Institute in the Melbourne Research office of the University of Melbourne, Australia. Our producers for this episode were Kelvin Param and Eric Van Bemmel, audio engineering by Craig

McArthur, theme music performed by Sergio Ercole. Melbourne University Upclose is created by Eric Van Bemmel and Kelvin Param. I!|m Jackie Angus, until next time, thank you for joining us. Goodbye.

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