

(Mr. WYNN addressed the House. His remarks will appear hereafter in the Extensions of Remarks.)

EMBRYONIC STEM CELL RESEARCH

The SPEAKER pro tempore. Under the Speaker's announced policy of January 4, 2005, the gentleman from Maryland (Mr. BARTLETT) is recognized for 60 minutes as the designee of the majority leader.

Mr. BARTLETT of Maryland. Mr. Speaker, very shortly now the juvenile diabetes people will be coming through the Congress. They do this every year, I believe.

I look forward to this visit with really mixed emotions. These children come in with this disease that has and will change their lives. Many of them are so brittle that they have to have a pump embedded under their skin that pumps insulin, because the sugar may go violently up or down with potentially disastrous effects on the person. Many times a day they may have to get a droplet of blood to determine the sugar level.

They will appeal to us, as they have every year for the past 5 years, please vote for Federal funds for embryonic stem cell research because they believe, like the loved ones of many other types of patients, that there could truly be miracle cures from embryonic stem cells. They will tell us that there are several hundred thousand embryos out there that are frozen in fertility clinics.

I have a daughter-in-law who is going through that process now. They harvest eggs. They fertilize the eggs. First, they have to give a hormone treatment to the prospective mother so that there will be the production of more than just the one egg that is produced normally per month. They will harvest a number of eggs, 8, 10, 12 eggs. Then they will fertilize those eggs, and they will watch their growth in the laboratory, and they will choose two or three of what look like the strongest fertilized eggs, and then they will implant those in the prospective mother.

The remaining eggs are frozen. It costs money to keep them there. The family may pay for that process because these little embryos that are implanted may not take, and they may need to do it again, and frozen, they could last quite a while, and they may want to have another child. So they will pay to keep them frozen for a while; but by and by, time and changes in the family, they will see no further need to keep them frozen. When they cease doing that, then the laboratory must either dispose of the embryos or bear the expense of keeping them frozen.

So each year a number of these embryos are discarded, and there has been an appeal, which has been bought into by some of my very good friends in the Congress, that from an ethical perspective, why should we not get some med-

ical use from these embryos that are going to be discarded anyhow.

That is a tough position to put pro-life people in, and the reason that most, but not all, pro-life advocates are opposed to this is because they view this as the beginning of a slippery slope. Today, you are permitting the use of surplus embryos that are going to be discarded anyhow; tomorrow, you might be producing embryos. They may be stronger, younger. You may be producing embryos just so you can discard them so you could use them for medical research.

I remembered the juvenile diabetes groups that come through, the children and their parents when, in 2000, I went to the National Institutes of Health when they had a briefing for Members of Congress and staff on embryonic stem cell research, the potentials and the challenge. There were a number of staff there. I think that I was the only Member of Congress who was there.

I went there from a somewhat unusual background, a different background than the average Member of Congress, because in a former life, I went to school and got a doctorate in human physiology. I got it not in a medical school but at an arts and sciences campus, and so we had to take a great variety of courses.

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Things like limnology and ichthyology and cytology and protozoology and advanced genetics. And one of the courses I took was advanced embryology. And in that course I had an opportunity to study and learn something about the process which is so familiar to anybody who has studied biology in life, that is, the development of the embryo and how this process goes.

I recognized that occasionally in humans in the early embryo, sometimes at the two-cell stage and sometimes later, and you can tell by how the babies present whether they share an amnion or simply share the chorion; how they present at birth you can tell at roughly what time in the development of the embryo did it split. And each of those halves of the original embryo, either one cell if it was a two-cell stage, or multiple cells if it was further along in the development before it split, each half produces what appears to be a perfectly normal baby. We call them identical twins. And there are tens of thousands of them out there and a great deal of scientific interest is in these twins.

And a lot of research has been done, because when you are looking at two genetically identical people, you have an opportunity to make some studies and observations that you would have to use a great many more subjects to make using the usual genetic different subjects.

And so recognizing that you could take half of the cells away from the original embryo and each half produced a perfectly normal baby, I rationalized,

gee, it ought to be possible to take a cell from the early embryo and it would not even know it. And that is because all the cells in the early embryo are what we call totipotent or at least pluripotent. Totipotent means they can produce another embryo if you take the cell out, and pluripotent means they can produce all of the cell types that make up the body. By the time they are pluripotent, they have lost the ability to coordinate all of the different kind of cells into an integrated individual, so they could not produce an embryo.

I asked the researchers at NIH, should it not be possible to take a cell from an early embryo without killing the embryo, probably without hurting the embryo, since in every set of identical twins half of the cells have been taken away from the embryo.

And by the way, Mr. Speaker, one of those is a clone. I guess you can decide which one of those identical twins you would identify as the clone, but clearly one of them is a clone, and both of them develop into what appears to be, by observations over hundreds of years and more recently many years of intensive physiological and medical observation, what appear to be perfectly normal human beings.

And so I asked the researcher at NIH, shouldn't it be possible to take a cell from an early embryo without killing the embryo, probably without hurting it? And they said, yes, they thought that should be possible. So a few days after that I happened to be at an event when the President was there, and I knew that he was laboring with a decision, a very difficult decision, of whether he was going to permit Federal dollars to be used in embryonic stem cell research when presently at that time the only source of embryonic stem cells resulted from the destruction of an embryo.

So I told the President about the meeting at NIH and about my discussion with the researchers there, and a few days later I got a call from Karl Rove. The President had remembered that conversation and turned the follow-up over to Karl Rove, and Mr. Rove told me that he had gone to NIH and had spoken with the investigators there, and they had told him that that was not possible. I said, Karl, either they are funning you or they misunderstood your question, because these are the same people that can go into an individual cell and take out the nucleus and put another nucleus in that cell. And they are telling you they cannot take a cell or two out of a big embryo?

So he went back and asked them again and came back and called me a second time and said, Roscoe, they tell me that they cannot do that. I wondered at the time what had happened. And a couple of years later, when the researchers at NIH were in my office, they somewhat sheepishly admitted that they had permitted Mr. Rove to believe something that wasn't quite true. Because what they had told him

was that they weren't sure that they could produce a stem cell line from a single cell taken from an early embryo.

That is exactly what my bill had proposed to do, was to determine, with animals, whether in fact that was possible or not. They had not meant for him to believe that it was not possible to take a cell from an early embryo.

Now, I cannot get inside their head to tell you, Mr. Speaker, why they permitted Mr. Rove to go away with this misconception. I can only tell you that I think that if I were in their place, I would have judged that the President might very well make the decision that it was okay to use these discarded embryos. Because, after all, they were going to be discarded anyhow, and the potential for life-saving medical applications was so great that I think that they may have rationalized that the President was going to issue an executive order which would make possible the use of Federal funds in the study of embryonic stem cells taken from these surplus embryos. That, of course, is not what the President did.

I am happy to be joined this evening by Dr. GINGREY, and I wanted to engage him in a dialogue, because I think that the same kind of an emotional response that might have permitted the researchers at NIH to permit this discussion to result in a misconception by Mr. Rove, that an analogous emotional response on the part of many pro-life advocates makes it very difficult for them to even talk about the potential of any form of embryonic stem cell research because they are so conditioned that the only way in the past that we have been able to get embryonic stem cells was by destroying an embryo, and so they equate any discussion of embryonic stem cell research as requiring the destruction of an embryo.

The President has a bioethics council that published a white paper in which they talked about four different techniques, potentially bioethically acceptable that could produce embryonic stem cells without destroying an embryo. And I wonder what is the best approach, because we want to carry everybody along with us. I want no one to be offended that what we are proposing, what has been proposed as a matter of fact by the President's council on bioethics is a violation of our fundamental belief that life is sacred. Every life is sacred, and particularly the least of these, this totally defenseless embryo. Their life is sacred, and we must protect that.

So the research that I am proposing, that my colleague has been supporting, does exactly that. And I am wondering what is the best way to bring this community along with us so that they understand that there are potential techniques that could be used for producing embryonic stem cells that will not consist of destroying or even hurting the embryo. What do you think is the best way to approach this?

Mr. GINGREY. Well, first of all, let me thank the gentleman from Mary-

land for his legislation, H.R. 3144, and for allowing me to spend a little time with him this evening as we try to explain to our colleagues what we are talking about here and what is the essence of the Bartlett bill.

I think the gentleman is correct that the perception among those of us who are strongly pro-life, and I think most of my colleagues on both sides of the aisle sort of know each other's former profession before we came to this august body, and I practiced medicine, not just an M.D., but specializing in obstetrics and gynecology; and so over a 26-year period, doing the average number of deliveries a doctor would do in a year, that amounts to over 5,000; and very proudly I can stand here tonight and say that I am pro-life and have never performed an abortion.

But I think that in response to the gentleman's question, people that are pro-life know that embryonic stem cell research that was ongoing before President Bush made his decision 2 or 3 years ago, that those stem cell lines were indeed obtained from this so-called excess. Really not excess. Cannot tell that to the Snowflake babies that have been adopted, those embryos, and there are close to 100 of those precious children alive today, but the pro-life community, indeed, everybody understood that the stem cell lines that were created were created from the destruction of embryos that were produced utilizing artificial reproductive technology that the gentleman from Maryland so adequately explained.

And of course those children, and I say children, they are embryos, but they certainly become children. They become fetuses, and they become children, and they become young adults, and they become middle-aged and senior citizens. They are human life. And, basically, what the President said is those that have already been destroyed to create these cell lines, we will allow researchers, our scientists, to apply for grants to conduct the research on those cell lines, those embryonic stem cells, but not to destroy any more life; to put a moratorium on that and to absolutely not continue to destroy life.

In fact, in 1999, President Clinton's National Bioethics Advisory Commission, NBAC, acknowledged broad agreement in our society that early human embryos "deserve respect as a form of human life." They recommended funding of embryonic stem cell research only if there were no alternatives. But what Congressman BARTLETT is talking about tonight, of course, is an alternative, a viable, if I can use that term, a viable alternative. And that is what he has outlined for us in this legislation, and I know he will talk about that.

But the important point is that people who are pro-life understand this, that taking a cell or two from an embryo, once it has gotten to the point where those cells are not totipotent, that you are not literally taking maybe something that in itself could

divide and become an embryo; you get beyond that stage to what he describes as pluripotent.

And the difference in those two capabilities in those embryonic cells is hugely important to the pro-life community. And he, of course, has done such a great job tonight, and I commend him for that, of explaining how in nature this occurs with the division of a multi-cell embryo to become identical twins; and it is, I think, a good explanation. And I think that is probably what is important, in response to your question, my good friend from Maryland, is this educational process.

And I know you have worked on this. I do not know how many times you have done this Special Order, but you have honored me in giving me an opportunity to participate with you and get into a colloquy and discuss some of these issues. This is the way to do it. This is the seed corn. This is what gets it started. It is a matter of understanding that there is an alternative to destruction of human life for the betterment of other lives.

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Mr. BARTLETT of Maryland. Dr. GINGREY, thank you very much.

There is another consequence of this understandable emotional reaction on the part of the pro-life community, and that is the statement that is made over and over again that we have, I think it is up to 70-some now, treatments or cures from adult stem cells and none from embryonic stem cells; therefore, why would you want to bother looking at embryonic stem cells?

The reason we have 70-some treatments from adult stem cells is we have been working with them for about 3 decades and we have been working with embryonic stem cells for just a little over 6 years. A newborn baby cannot run a marathon, and there just has not been time for the medical community to develop the potential from embryonic stem cells.

I will be the first to tell you that this research may be very disappointing. I hope that it will not be, because these cells really want to divide, and like an obstreperous teenager, they may be very difficult to control. But the hope is that since embryonic stem cells can certainly make any and every tissue and, potentially, organ in the body, they ought to have the greatest potential.

And I wonder what we need to do so that the statement is not repeated that it is really silly to talk about embryonic stem cell research because we have 70-some treatments or cures from adult stem cells and none yet from embryonic stem cells. That is, of course, a true statement, but you need to put it in context. The reason for it is we have been working for more than 3 decades with adult stem cells and just a little over 6 years with embryonic stem cells. And I want our community to have credibility at the end of the day.

How do we meet this emotional challenge?

Mr. GINGREY. Mr. Speaker, if the gentleman will yield, I think it really is a good point that you are making that we have been utilizing adult stem cells for a long time, for many years, and whether we are talking about cells that are obtained from bone marrow or from blood, even, of course, some umbilical cells. But as the gentleman points out, there have been some real great success stories reported: cancers, including ovarian and testicular cancer; leukemia; Hodgkin's disease; stroke; heart disease; Parkinson's disease; as the gentleman mentioned, juvenile diabetes; Crohn's disease, an inflammatory disease of the bowel which can be so devastating.

And I think ROSCOE BARTLETT, the gentleman from Maryland, mentioned maybe 58, in total, success stories. But the earliest cell, I think, has the greatest potential, and that is basically the point that the congressman is making and why his bill, H.R. 3144, to provide funding, very necessary funding, to do the basic and applied research starting in animal models to show that you indeed can take these, again, not totipotent but pluripotent, so not another embryo, but something that has gone beyond that stage that does not have the capability in and of itself of becoming a human being. That is what we want to say to the pro-life community.

So we are taking, though, the very earliest beyond that stage cell, and there is no telling what tissue it can develop into, whether we are talking about brain tissue and trying to treat people, God rest his soul, like Christopher Reeves or other people with spinal cord injuries, or someone with severe Parkinson's disease or Alzheimer's or juvenile diabetes where you create islet cells that you can transplant into a person's pancreas that, because of a genetic defect, has no islet cells.

So that is really, I think, the answer, to say why it is worth the effort, why it is absolutely worth the effort. First and foremost, you do not have to take human life for the betterment of other human lives, and we want to build on the success of utilization of adult stem cells and go that extra mile, and this is what this bill will do, allow us to do the basic research, fund it with Federal dollars so we can get to that point.

Mr. BARTLETT of Maryland. Thank you very much. I appreciate your mentioning the diabetes, particularly juvenile diabetes.

The deficiency, of course, is in the Islet of Langerhan cells, named after the German scientist who first saw them. They are like little islands scattered through the pancreas. I have no idea why they are in the pancreas. They have no relationship to the physiology of the pancreas; they just happen to be there, and they are not producing enough insulin. But replacing the insulin does not cure diabetes because the person who has diabetes will end up with eye problems, circulatory problems, toes that they lose, gangrene, and so forth.

And these children now are starting out with the absolute certainty that they are not going to have the quality of life of other children because just replacing the insulin does not cure diabetes. It controls many of the effects, but there will still be consequences to the diabetic.

And as you mentioned, there is the hope that with embryonic stem cells we could grow Islet of Langerhan tissues. And you would not have to put those back into the pancreas. You could, as a matter of fact, put them in the groin or under the arm or under the skin, anywhere. They just have to have access to circulation. They will produce the insulin. The circulation will pick up the insulin, and then it flows to the liver and the cells of the body where it does its miracle work.

But this is the reason that they are so enthusiastic about embryonic stem cell research, because of all of the diseases out there. And we spend more money on diabetes than any other disease in the country, and there is probably more debility and suffering from diabetes than any other disease in the country. And that is why they are so adamant in their desire that we permit Federal dollars to be spent, because with the power of NIH and the peer review, and they have created miracles in the past, they hope they can do another one.

I would like to just look for a moment at the physiology, and the chart, boy, this is really abbreviated. I will show you a little more expanded one in a moment.

But the two gametes come together and produce what is called a zygote, and this is the fertilized cell. It now has half the genes from the mother and half the genes from the father. And then that fertilized cell grows through several stages, and they have skipped the morula stage here and they go right to the blastula and then to the gastrula. And here you start the differentiation into the three germ layers.

Every tissue of our body develops from one of the three germ layers: the endoderm, that is what is inside; and the mesoderm, that is what is in the middle; and the ectoderm. Very interestingly, the parts of the adult body that develop from ectoderm is our skin and our nervous tissue. Most of this, by weight, develops from mesoderm. All the muscles, all the bones develop from mesoderm. And here you see at the bottom are derivatives of the ectoderm and the mesoderm and the endoderm, and then the unique cells, the germ cells, the sperm in the male and the egg in the female.

Now, adult stem cells, when you hear people talk about adult stem cells, what they are talking about is a cell down here, and one of the easiest ones to talk about are adult stem cells that have to do with making blood, and these stem cells found in the bone marrow primarily can produce a variety of cells. The polymorpho-nuclear leukocytes, the erythrocytes, the

thrombocytes, all of those can be produced.

Now, you can take an adult stem cell and trick it into believing that it has not gone through all of this differentiation, that it is somewhere back here so that it can now make tissues other than just the ones that it was destined to make and the organ from which you took it. And these are the techniques that are used in adult stem cell research and treatment.

The next chart shows a little more detail in this development process, and this shows it in the reproductive tract of the female. Here is the ovary from which the egg is released. And the egg now starts a long journey down through the fallopian tube. It will be 7 to 10 days before it finally implants in the uterus. The sperm, of course, makes its way from the vagina up through the uterus and through the fallopian tube, and it fertilizes the egg. It shows it very correctly here. Fertilization occurs well up in the fallopian tube. A little later down and it cannot be fertilized.

And this shows the production of the zygote. It shows the first cleavage to produce a two-cell mass. At this point these two cells could separate to produce two embryos, two babies. We know them as identical twins. Or it can go on to split into four cells and eight cells, and I will come back to the eight cell in just a moment because that is the one medically that is of considerable interest.

Then it becomes a morula. You see it there, the compacted morula. And then you get the inner-cell mass, which you saw a pretty good picture of in the previous slide. And, of course, what we are talking about is what goes on in the laboratory now in a petri dish. You fertilize it there rather than in the reproductive tract, but the same sequence of development occurs. And they simply take the inner-cell mass out of the embryo and squash it and kill it and take the cells out to produce a stem cell line.

In the laboratory, in in vitro fertilization, they grow the embryos up to the eight-cell stage, and it is at that stage that they have the most luck in implanting them in the uterus of the female. Several years ago in England, a clinic there began taking a cell, and sometimes they got two, from the eight-cell stage, and they did a preimplantation genetic diagnosis on it because if you had the option of making sure that your baby was not going to have a genetic defect like trisomy 21, mongolism, for instance, you certainly would want to avoid that if you could.

They do a preimplantation genetic diagnosis, and if there is no genetic defect, they then take the remaining six or seven cells and implant them, and now worldwide I suspect there have been more than 2,000 babies born.

There is a clinic just outside Washington, in Virginia, and a year ago I spent more than a half hour talking

with two of the physicians there who have been doing this technique. So we now are producing babies with this technique, with the assurance that there will not be any genetic defects.

Another really good use of that cell that you take from that, and I have to credit Mr. Dorflinger with this, the spokesman for the Conference of Catholic Bishops, and he suggested that the most ethical reason for taking a cell from the early embryo, even more ethically defensible than doing a preimplantation genetic diagnosis, would be making a repair kit. That is sort of the goal when you freeze the cord blood, and we had a bill that everybody but one voted for that gave Federal dollars for freezing cord blood.

Those will not be embryonic stem cells. They will be adult stem cells, but at least they are closer to the genetic identity of that person than other cells would be. And more than 2,000 times worldwide now we have had a perfectly normal baby from that process.

So what I had proposed to the people has, in fact, been done. And what I envision at the end of the day in our bill, H.R. 3144, does not support experimentation in humans. It is only animal experimentations to verify that these procedures are, in fact, doable and efficacious and that the embryo is not harmed.

□ 2115

This technique and three other techniques are included in the white paper prepared by the President's council on bioethics, alternative sources of human pluripotent stem cells.

Dr. Gingrey mentioned totipotent and pluripotent, and I would like to spend a moment talking about that. Totipotent means that the cell you take could produce another embryo. Pluripotent means that it could produce all the cells, tissues, organs of the body; but it does not have the capability to organize them into a person. Ethically, if you took a cell that was totipotent, you would simply be creating a new embryo, and so the argument starts all over again. So you need to take a cell from a stage where it is just pluripotent, not totipotent.

I am assured by the research community that no one has ever been successful in developing an embryo with a cell taken from the eighth stage. You see, these cells know, and I use that term advisedly, know that ultimately they are going to differentiate, and apparently that differentiation problem has started well before you see the three germ layers developing, because between the fourth stage and the eight-cell stage, they have lost their ability to be totipotent. They can now only be pluripotent. As Dr. Gingrey pointed out, it is very essential that ethically you take cells that could only be pluripotent.

I have two quick slides here that look at the development of twins. This is the two intercell masses. These are when the twins develop, the identical

twins develop later, when it splits later. You can see that because they each have their own amnion. They share a chorion, of course, but they each have their own amnion.

Let me see the next one, which shows how you have what are called fraternal twins. Here you have two eggs produced by the mother, ordinarily only one, sometimes two, sometimes three, but ordinarily only one egg, unless you are giving some hormone treatment. Then those are now presented in separate chorions. They, of course, have their own amnion, which is the tissues around the baby which contains the fluid in which the baby floats, and the tissue around that is called the amnion.

There are four techniques in the white paper. I would like to look at the technique that I have been looking about. Number two in the white paper.

They credit me with suggesting that. There is a little footnote: "A similar idea was proposed by Representative ROSCOE BARTLETT of Maryland as far back as 2001," and I think I actually talked to the President before that. They say it may be some time before stem cell lines can be reliably derived from single cells. We have two investigators, Landry and Verlinsky, who claim that they have done that.

You see, these cells love company, and they don't behave well if they are alone and they don't have company, so that is why there was the concern that maybe you could not develop an embryonic stem cell line from a single cell. But these two investigators have done it in a very clever way. They provide company for the cells, and then they separate the company, these are other types of cells, they separate the embryonic cells from the other cells that provided company for them to encourage them to continue the division process.

A second technique, as a matter of fact it was number one, mine was number two, the first technique that they talked about is a really interesting one. What this does is to propose the use of cells from an embryo much like we use organs from a cadaver. Everybody is familiar with that, and there are many people that have a will that say you can harvest their organs to benefit somebody if that would be useful.

When you create these embryos in the laboratory, not all of them are robust. A fair percentage of them never make it. They divide through a few stages for a few days and then just die. This proposal is if you determine that the embryo is moribund, and there is pretty good scientific evidence that you can do that with quite some certainty, kind of equivalent to determining a person is brain dead and therefore there is no chance that they can go on with life as we know it, and his proposal is that if you determine that the embryo is not going to make it, that it will die, but before it dies, you then take a cell or cells from the

embryo to create an embryonic stem cell line. This is very equivalent to taking organs from a cadaver.

There may be some question as to whether you can get a really good strong cell from an embryo that is in a day or two going to be dead, but it is possible that you could do that. My bill actually asks for Federal dollars to explore all of these techniques with animal models.

I was talking to one of the researchers, Dr. Hurlbut, the other day. This is Dr. Landry's proposal. I noted that I would be enormously surprised if what we found in the great apes was not going to be what we found in humans, and he agreed that he too would be enormously surprised.

It may be somewhat humbling, but we share a vast majority of our organs with the great apes, the chimpanzees and orangutans and gorillas. You have to look to see genetic differences. They have the same number of chromosomes, and we share many, many, most, 90-odd percent of all the chromosomes. So it would be very unlikely that what we found in animals would not occur in humans.

We have a couple more charts that address this. There has been a lot of thought given to this, and I think that we have one; let's look at the one that actually shows the depiction, yes, that one. Let us look at that one.

That shows what happens in these cells, these embryos, in just a couple of days. They go from a perfectly normal looking embryo to a dead embryo, but there are clues that that is a certain result that the experts can see in these cells.

So this is a potentially viable, I believe ethically acceptable technique, very analogous to taking organs from a cadaver. This is simply taking cells from what would be the equivalent in an embryo of a cadaver, an embryo that will not live, that will die.

There is another technique, and I would like to submit two papers here for the RECORD, and these are papers describing another technique, a very interesting one. This is Dr. Hurlbut's contribution.

Researchers can take an oocyte, that is the egg from a mother, and they can take the nucleus out of that oocyte and place a nucleus from an ordinary cell, like a skin cell, inside the cell, and then with a little shock treatment you can trick the cell into believing that it was fertilized, and it will go on to develop into an individual. That is how we got Dolly the Sheep. It is called cloning.

Dr. Hurlbut's suggestion is, and this is called epigenetic nuclear transfer, that he alters that. The nucleus that you place in the cell has an induced genetic defect. They alter one of the genes so that the result cannot produce an embryo.

There are things that happen in some mothers where you have growths and they will have teeth and hair, but it certainly is not a baby. It is not coordinated. You can turn off this gene so

that what you have produced is not an embryo, could not be a baby.

It is very interesting that the way you turn that off is by RNA, ribonucleic acid, rather than deoxy ribonucleic acid, which is what is in the nucleus and what makes up the genes and chromosomes. The RNA is out in the cytoplasm, and I am not so sure that a clone is going to be that identical to the original because the RNA, the cytoplasmic RNA, is going to be different; and the cytoplasmic RNA has a big influence because it can turn on and turn off genes. This is the technique used for doing this.

This, I think, is from *Nature Magazine*, one of the premier scientific journals. It is the British equivalent to our *Science Magazine*. It is really multidisciplinary and very discriminating in the articles that it prints.

The bottom sequence here shows what he would do. He is producing something that cannot be a baby because the gene that is responsible for the organization of these various types of cells into a coherent human being is turned off. By the way, whether he turns that off in the cytoplasmic nucleus before he puts it in the cell so you avoid the argument that you are altering an embryo, because it is not an embryo, it is just a nucleus from a skin cell and he turns off the gene there, and then he takes the cell out of an oocyte and places this nucleus from the skin cell with the genetic alteration, places it in there. This is also a potentially viable technique.

All of these, by the way, you can argue that you may have some ethical problem with it. You may argue that you are intentionally creating a freak here just so you can harvest the cells from it. But since you are doing this before you place the nucleus in the oocyte, you are simply altering the nucleus in a skin cell, I think you can get by the ethical arguments.

Let us go back for a moment to the ethical arguments, because they are very important. I want to make sure that sensitivities of nobody in the pro-life community are violated.

The technique that I suggested to the President and the one that is described in our bill, we would not get the stem cells until several things had happened over which we have no control and no influence. The first thing is that a couple has decided that they are going to do in vitro fertilization. In addition, they have decided that they want to create a repair kit for their baby. They may or may not decide that they want to do a pre-implantation genetic diagnosis.

By the way, you can do both of those in the same cell. You simply culture the cell and you have now more than one, ultimately many, so you can take a cell for pre-implantation genetic diagnosis. They will have made the decision they want a repair kit. All we are asking for is a few surplus cells, one will do, a few would be better, a few surplus cells from their repair kit.

What this would do is provide for that baby, then a child, then an adult, throughout its life the potential that if it had diabetes, you could develop other Langerhans cells from its repair kit that are genetically absolutely identical to the person so there would now be no threat of rejection. This would clearly, clearly be miracle medicine.

I think we have gotten by the ethical objections, because whether or not you believe that parents ought to use in vitro fertilization, these parents have decided to do that. Whether or not you believe they should take a cell to produce a repair kit, these parents have decided to do that. So they have already made those two decisions, both of which I think are ethical.

□ 2130

Parents really want a child when they will go to the extent of in vitro fertilization. As I mentioned, my daughter-in-law is going through that. And after the surgery for harvesting of the cells, she cannot even drive a car for quite a while. This is not a casual procedure.

So these are loving parents who want a child. And I think it would be very rational that they would want that child to have a repair kit if they could, and we are simply asking for a few surplus cells from the repair kit.

I should mention the fourth procedure that is in this white paper, and that is the dedifferentiation of the adult cells. This dedifferentiation is a play on differentiation, and what happens is that the single cell produced by the union of two gametes, called the zygote, this cell now differentiates. It produces tissues that are endoderm, from which the lining of your intestinal tract and lungs and the lining of your blood vessels will come, the mesoderm and so forth. So they have differentiated.

You can now potentially get the equivalent of an embryonic stem cell if you can simply take one of these adult cells and trick it into believing that it has not differentiated. What you will do is dedifferentiate it.

I do not know how consistently you can do that, but that is why we need to do the research. On occasion you can do that, and I do not know how consistently you can do it. I do not know how viable the tissues will be once you have done it, but that is the reason that you do research.

I would just like to again mention that our bill, 3144, does not provide any Federal funds for any work on humans. It is only animal experimentation. And it would provide Federal money for working on all of the techniques that the President's Council on Bioethics indicated might be ethically acceptable under the right circumstances.

Of course, one of the things that is very much involved in whether it is ethical or not is, does it do harm to the baby? And that is why the animal experimentation first. We want to make

sure that in fact these techniques can occur. We want to make sure that there is no negative effect on the embryo.

There should not be, Mr. Speaker, unless you think that identical twins are somehow deficient, there should not be any medical effect, because we have, over hundreds of years, tens of thousands of identical twins, all of which appear to be perfectly normal human beings.

The potential for healing, medical applications in embryonic stem cells is just incredibly great, which is why the big interest in this. It is why the people at NIH would really like funding for this. It is why the groups that will come to see us, the juvenile diabetic groups that come to see us, will be advocating so strongly for research with embryonic stem cells, because this really could be a big, big breakthrough.

It could provide miracle cures that we can only dream of today. We need to make very sure that we are not crossing ethical bounds, that we are purely ethical.

Mr. Speaker, I am very concerned that none of my friends in the pro-life community be offended by any of this research, which is why the animal experimentation first, with a clear bioethical look at this.

I appreciate very much this opportunity to discuss this. Mr. Speaker, I include for the RECORD the articles I referenced earlier.

PRODUCTION OF PLURIPOTENT STEM CELLS BY OOCYTE ASSISTED REPROGRAMMING

As described in the President's Council on Bioethics' recent White Paper, altered nuclear transfer (ANT) is a broad conceptual proposal for producing pluripotent stem cells without creating and destroying embryos. In the description set forth below, we outline a research program for a form of ANT that should allow us to produce pluripotent stem cells without creating or destroying human embryos and without producing an entity that undergoes or mimics embryonic development. The method of alteration here proposed (oocyte assisted reprogramming) would immediately produce a cell with positive characteristics and a type of organization that from the beginning would be clearly and unambiguously distinct from, and incompatible with, those of an embryo. Incapable of being or becoming an embryo, the cell produced would itself be a pluripotent cell that could be cultured to establish a pluripotent stem cell line. Significantly, this cell would not be totipotent, as a zygote is.

Our proposal is for initial research using only nonhuman animal cells. If, but only if, such research establishes beyond a reasonable doubt that oocyte assisted reprogramming can reliably be used to produce pluripotent stem cells without creating embryos, would we support research on human cells.

With few exceptions all human cells contain a complete human genome, i.e. the complete DNA sequence characteristic of the human species. Specifically, one-celled human embryos, pluripotent human embryonic stem (or ES) cells, multipotent human adult stem cells, and differentiated (specialized) adult human cells such as neurons all contain a complete human genome. Thus, possession of a human genome is a necessary but not sufficient condition for defining a

human embryo with its inherent dignity. Rather the nature of each cell depends on its epigenetic state, i.e. which subset of the approximately thirty thousand human genes is switched on or off and, if on, at what level. For example, the gene for albumin, a liver specific protein, is found both in human embryos and in adult human liver cells called hepatocytes. However, neither the messenger RNA (mRNA) for albumin nor the protein itself is found in single-celled embryos because in them the gene is silenced.

This fundamental observation has given rise to the concepts of cell fate plasticity and epigenetic "reprogramming." If successful, reprogramming converts a cell from one kind to another by changing its epigenetic state. The ability to clone animals, such as Dolly the sheep, by transfer of a specialized adult nucleus to an enucleated oocyte demonstrates the power of epigenetic reprogramming: the oocyte cytoplasm is sufficient to reprogram the somatic nucleus to a totipotent state. Human cloning has been proposed as a means of generating human embryos whose pluripotent stem cells would be used in scientific and medical research. Here, through a form of altered nuclear transfer, we propose to utilize the power of epigenetic reprogramming in combination with controlled alterations in gene expression to directly produce pluripotent cells using adult somatic nuclei, without generating and subsequently destroying embryos.

How do pluripotent stem cells differ from totipotent single-celled embryos? Several key transcription factors essential for establishing and maintaining the pluripotent behavior of ES cells have been identified. Importantly, some of these are specifically expressed only in pluripotent cells, such as embryonic stem cells or the cells found in the inner-cell-mass (ICM) of the week-old embryo or blastocyst. They are not expressed in oocytes or single-celled embryos. Expression of these factors therefore positively defines and distinguishes mere pluripotent cells from embryos. These factors instruct a cell to have the identity of a pluripotent cell. Currently, the best studied example is the homeodomain transcription factor called *nanog* (Mitsui, Tokuzawa et al. 2003*). *Nanog* is not present in oocytes or single-celled embryos, but first becomes expressed weakly in the morula and then highly in the ICM (Mitsui, Tokuzawa et al. 2003; Hatano, Tada et al. 2005). Deletion of *nanog* does not prevent early cleavage stages of embryogenesis including formation of the ICM but does prevent the formation of an epiblast (Mitsui, Tokuzawa et al. 2003). ES cells in which *nanog* is blocked lose their pluripotency—which clearly shows that *nanog* is a positive factor instructing cells to be pluripotent, i.e. to behave like an ES cell. Furthermore, ES cells which constitutively express *nanog* can no longer be differentiated, i.e. are forced to remain in their undifferentiated state (Mitsui, Tokuzawa et al. 2003).

We propose a procedure that combines epigenetic reprogramming of a somatic nucleus with forced expression of transcription factors characteristic of embryonic stem cells, to produce a pluripotent stem cell. As a result of this procedure, *nanog* and/or other, similar factors, would be expressed at high levels in somatic cells prior to nuclear transfer, to bias the somatic nucleus towards a pluripotent stem cell state. Such altered nuclei would then be epigenetically reprogrammed by transplantation into enucleated oocytes. Alternatively or concomitantly, the mRNA for these same factors could be introduced into the oocyte prior to nuclear transfer. This procedure could ensure that the epigenetic state of the resulting single cell would immediately be different from that of an embryo and like that of a pluripotent

stem cell: the somatic-cell nucleus would be formed into a pluripotent stem-cell nucleus and never pass through an embryonic stage. Therefore, unlike some other proposed methods of ANT, this method would achieve its objective not by a gene deletion that precludes embryonic organization in the cell produced, but rather by a positive transformation that generates, *ab initio*, a cell with the distinctive molecular characteristics and developmental behavior of a pluripotent cell, not a totipotent embryo. This should allow us to produce a pluripotent stem cell line with controlled genetic characteristics.

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RESEARCHERS OFFER PROOF-OF-CONCEPT FOR ALTERED NUCLEAR TRANSFER

CAMBRIDGE, MA, Oct. 17, 2005.—Scientists at Whitehead Institute for Biomedical Research have successfully demonstrated that a theoretical—and controversial—technique for generating embryonic stem cells is indeed possible, at least in mice.

The theory, called altered nuclear transfer (ANT), proposes that researchers first create genetically altered embryos that are unable to implant in a uterus, and then extract stem cells from these embryos. Because the embryos cannot implant, they are by definition not "potential" human lives. Some suggest that this would quell the protests of critics who claim that embryonic stem cell research necessitates the destruction of human life. Scientists and ethicists have debated the merits of this approach, but so far it has not been achieved.

"The purpose of our study was to provide a scientific basis for the ethical debate," says Whitehead Member Rudolf Jaenisch, lead author on the paper that will be published in the October 16 online edition of the journal

Nature. "Our work is the first proof-of-principle study to show that altered nuclear transfer not only works but is extremely efficient."

First proposed by William Hurlbut, Stanford University professor and member of the President's Council on Bioethics, ANT has been described as an ethical alternative to somatic cell nuclear transfer (SCNT), also known as therapeutic cloning.

For SCNT, a donor nucleus, for example one taken from a skin cell, is implanted into a donor egg cell from which the nucleus had been removed. This egg cell is then tricked into thinking it has been fertilized. That causes it to grow into a blastocyst—a mass of about 100 cells—from which stem cells are removed. These embryonic stem cells can divide and replicate themselves indefinitely, and they can also form any type of tissue in the human body. However, to cull these stem cells, the blastocyst must be destroyed, which some critics insist is tantamount to destroying a human life.

The procedure theorized by Hurlbut is similar to SCNT, but with one crucial twist: Before the donor nucleus is transferred into the egg cell, its DNA is altered so that the resulting blastocyst has no chance of ever becoming a viable embryo. As a result, a "potential human being" is not destroyed once stem cells have been extracted.

Jaenisch—a firm supporter of all forms of human embryonic stem cell research—has shown that technical concerns about this approach can be overcome.

Jaenisch and Alexander Meissner, a graduate student in his lab, focused on a gene called *Cdx2*, which enables an embryo to grow a placenta. In order to create a blastocyst that cannot implant in a uterus, the researchers disabled *Cdx2* in mouse cells.

They accomplished this with a technique called RNA interference, or RNAi. Here, short interfering RNA (siRNA) molecules are designed to target an individual gene and disrupt its ability to produce protein. In effect, the gene is shut off. Jaenisch and Meissner designed a particular form of siRNA that shut off this gene in the donor nucleus and then incorporated itself into all the cells comprising the blastocyst. As a result, all of the resulting mouse blastocysts were incapable of implantation.

However, once the stem cells had been extracted from the blastocysts, *Cdx2* was still disabled in each of these new cells, something that needed to be repaired in order for these cells to be useful. To correct this, Meissner deleted the siRNA molecule by transferring a plasmid into each cell. (A plasmid is a unit of DNA that can replicate in a cell apart from the nucleus. Plasmids are usually found in bacteria, and they are a staple for recombinant DNA techniques.) The stem cells resulting from this procedure proved to be just as robust and versatile as stem cells procured in the more traditional fashion.

"The success of this procedure in no way precludes the need to pursue all forms of human embryonic stem cell research," says Jaenisch, who is also a professor of biology at MIT. "Human embryonic stem cells are extraordinarily complicated. If we are ever to realize their therapeutic potential, we must use all known tools and techniques in order to explore the mechanisms that give these cells such startling characteristics."

ANT, Jaenisch emphasizes, is a modification, but not an alternative, to nuclear transfer, since the approach requires additional manipulations of the donor cells. He hopes that this modification may help resolve some of the issues surrounding work with embryonic stem cells and allow federal funding.

This research was supported by the National Institutes of Health/National Cancer Institute.

BLUE DOG COALITION AND THE BUDGET

The SPEAKER pro tempore (Mr. DAVIS of Kentucky). Under the Speaker's announced policy of January 4, 2005, the gentleman from Arkansas (Mr. ROSS) is recognized for 60 minutes as the designee of the minority leader.

Mr. ROSS. Mr. Speaker, I rise this evening to talk about our budget, to talk about our debt, to talk about our deficit.

As a member of the fiscally conservative Democratic Blue Dog Coalition, a group of 37 fiscally conservative Democrats, we are here as a group to hold our government accountable for the reckless spending, the record deficits, and the lack of fiscal discipline that we see in our Nation's government these days.

A good example of that, Mr. Speaker, can be found in my district, in fact, in my hometown where I grew up and finished high school, Hope, Arkansas. As you may know, we had the most costly natural disaster ever in our Nation's history hit us about 6 months ago, that of course being Hurricane Katrina.

Mr. Speaker, let me tell you that my heart goes out for the victims of Hurricane Katrina, many who remain homeless today. I am real proud of the people of my congressional district, the 4th District of Arkansas, who opened up their arms and their homes and their communities. Some people referred to them as evacuees. We called them our neighbors, our neighbors from Louisiana and Mississippi who came to Arkansas to seek refuge.

A few weeks, perhaps a couple of months, after Hurricane Katrina, FEMA, the Federal Emergency Management Agency, showed up at city hall in Hope, Arkansas, and explained that they were aware that Hope owned an old World War II airport, airfield and accompanying pasture, and they understood that many of those runways were now inactive. And they proceeded to explain how they were buying some 20,000 manufactured homes, and they wanted to use the old World War II airport, the inactive runways at the airport there in Hope, Arkansas, as what they called a FEMA staging area, and that manufactured homes and they would be coming and they would be going, going to the people who lost their homes and everything they owned in Louisiana and Mississippi.

Well, Mr. Speaker, they did come. Here is an aerial photo of what has come to Hope, Arkansas. According to FEMA's most recent count, 10,777 manufactured homes have come to this so-called FEMA staging area in my hometown where I grew up, Hope, Arkansas. I now live some 16 miles from there in Prescott.

I have been there, Mr. Speaker. I have seen these 10,777 manufactured homes. They came. But not a single one left, not one. Not one home left for the people they were intended for. To put it another way, it is \$431 million worth of manufactured homes sitting in a cow pasture in Hope, Arkansas.

Now, originally what FEMA had intended to do was use this as a staging area and homes would be coming and homes would be going. They would have room for them on these inactive runways. But today only 25 percent of them sit on these inactive runways. As you can see, many of them, in fact 75 percent of them, are sitting in cow pastures around the airport.

If you were to stack these manufactured homes, a few of them are 80 feet long, most of them are 60 feet, if you were to stack them end to end, they would stretch 172 miles. They would stretch from the Texas-Arkansas border at the Red River all of the way to the Arkansas-Mississippi border at the Mississippi River.

These manufactured homes, every single one of them, are fully furnished, beds, mattresses, box springs, dining room, sofa, end tables, coffee tables, fully furnished. Yet at the same time, FEMA has announced that they are planning on March 1 to evict, or in early March, they plan to evict some 12,000 people from hotel rooms, and yet FEMA is sitting, sitting on 10,777 brand-new, fully furnished manufactured homes. They are just sitting on them at the Hope airport in Hope, Arkansas, some 450 miles from the eye of the storm.

Stanley McKenzie is from the New Orleans area. I have been talking with Stanley. Stanley is one of the victims of Hurricane Katrina who, some 6 months after the storm, remains in a hotel room in Monticello, Arkansas. Stanley and I talked this evening. Stanley explained to me that he did not want to be in a hotel room. He wanted to be in a manufactured home and has a location in Monticello to put one of these manufactured homes which are being stored about 2 hours west of Monticello.

And yet FEMA says he cannot have one. FEMA says he cannot borrow one for the next 18 months, as the program calls for.

They do not give these things away. They let people use them for up to 18 months, which is a whole other issue; that being, FEMA says the 18 months start from the date of the Federal declaration, not the date that the people actually receive the home. So every one of those 10,777 homes have an expiration date on them. The date does not begin, the 18-month window for people to live in them while they try to sort through their life and find a place to live after losing everything they own in Hurricane Katrina, does not start from the time they receive a home, it starts from the time of the Federal declaration.

So each day those homes sit at the airport and at the pasture in Hope is a day that no one can ever live in them. So I am calling on FEMA to revise their policy for the 18 months to begin at the time in which people are able to actually obtain one of these homes.

Now, what they tell Stanley is, he cannot have one, even though he has