

Below is the transcript of your testimony before the Morella's Science Committee hearing on March 5, 1997, called "Biotechnology and the Ethics of Cloning: How Far Should We Go?"

Mr. VARMUS. Thank you, Madam Chairwoman. I would like first, on behalf of my colleagues, to thank you for holding this important hearing.

As President Clinton said yesterday, all Americans, including the Clintons, are spending a great deal of time around the dining room table talking about these issues. We see these issues as important topics for conversation so that policy gets set properly. And, we also see it as an opportunity to educate the public about the excitement in biological science.

In my brief remarks, I am going to touch on three things. I would like to review very briefly some of the foundations of the science that allowed the experiment that brought us all together to actually occur.

Secondly, I would like to talk about the future applications of these breakthroughs and to do that in a way that sets the stage for the conversations we will have together with my other panelists.

And, lastly, I would like to speak very briefly about some of the steps that have been taken by the Administration in view of the recent discoveries.

The science that we are talking about has a very rich and deep history. Indeed, it was nearly 60 years ago that the famous German embryologist, Hans Spemann, first proposed the notion of nuclear equivalence.

To understand what that phrase means, let us think about a very simplistic view of mammalian development, as shown by the figures on the left side of the chart in the front. After a sperm and an egg, each carrying genes from the mother and father, are fused, a series of cell divisions gives rise to a very primitive embryonic form called the blastocyst, which then develops into an early embryo, and then into a late embryo and then into a fetus, and finally, after several months in the uterus of a mother, produces a newborn and then an adult animal.

During the course of these complex events, which ultimately give rise to a complex organism with many different kinds of cells and tissues, the roughly 80,000 genes that are housed in the nucleus are turned on and off in a series of events that are orchestrated in an extremely complex way. Spemann asked: Could the collection of genes housed within the nucleus of any single cell be competent to give rise to an entire new individual?

Over the course of the last couple of decades, in work with frogs and a variety of animals, that question has been put to a test, using as sources of nuclei at least the four kinds of--or four forms of mammalian organisms shown on the left--that is, cells from very immature embryos, from late embryos, from the fetuses and from adults. Those cells, either directly taken from the blastocyst or grown temporarily in culture, provided the source, the donors, for the nuclear transfer experiments.

The recipient cell in these experiments is an egg from which the nucleus, shown by the pink dot in the center of the drawing, has been removed using a micropipette, a fine needle. That cell, now deprived of its own nucleus, is the place into which the donor nucleus in the donor

cell is provided by, first, an injection and then a fusion event that can be initiated, for example, by an electric shock.

It's intended that the fused cell then undergo divisions into a multiple cell aggregate that resembles the blastocyst, as normally occurs. And, that blastocyst can then be implanted into the uterus of a surrogate mother in which further developmental events occur and, ultimately, progeny results.

Now, a number of laboratories over the last decade or so have shown--with a variety of animals, including sheep, pigs and most recently, as you will hear soon from Dr. Smith, rhesus monkeys--have given rise to animals from--by nuclear transfer from blastocysts. What, of course, is extremely remarkable about Dr. Wilmot's experiments was the use of later embryos, fetal cells and, in one case, as you have described, Madam Chairwoman, from an adult mammary gland and transferred using some novel technologies was capable of giving rise to a mature animal.

Let me speak briefly to the implications of this science. First, in the area of traditional husbandry, we know throughout the history of man, as an agricultural animal that many techniques have been used to generate optimal forms of plants or animals for feeding the human population. Dr. Rexroad will describe some of those and show how these new techniques could fit into our traditional concepts of husbandry designed, as would be the self-fertilization or corn with the twinning of cows or sheep as a technique for improving the vitality of our agricultural industry.

The second application is in the area of what I would call non-traditional husbandry, husbandry in which the animals that are being used have been modified by genetic technology that Mr. Brown referred to in ways that allow the production of medically useful products or organs that might be suitable for human transplantation.

And, Dr. Geraghty will address some of those applications.

The third application is in the area of research on human disease, in the area of developing models for human disease. As you are well aware, Madam Chairwoman, for many years, investigators have used mice and rats and sometimes other laboratory animals to study a variety of human diseases.

Recently, it has been possible to modify the chromosomes of mice using advanced recombinant DNA technology to try to mimic some of the genetic diseases that occur in such animals. While the genetic manipulations are possible, the mice that result from them do not always accurately mimic the disease that one intends to study.

Therefore, the possibility of making such manipulations in other kinds of animals and cloning such animals for the purpose of studying diseases like cystic fibrosis and others is made more possible by some of the technologies we will be discussing. Dr. Smith, in her discussion of the generation of--of genetically identical rhesus monkeys will specifically address this in the context of many diseases, including AIDS, that we are concerned about.

The fourth general area of application addresses questions about fundamental biological principles. I mentioned earlier that during the generation of mature animals, there is a ballet going on in which subsets of our genes are turned on and off in an orchestrated display that underlies many diseases as well as developmental processes.

Understanding how such control occurs, how genes that are told to be off can be once again told to be switched on and vice-versa, will have deep implications for our understanding of mammalian development, aging and many other processes.

Understanding these issues, the answers to such fundamental questions, will, I believe, affect a fifth area of concern; and, that is the reprogramming of human cells to treat certain diseases. We already use such a principle in trying to treat sickle cell disease.

A gene called the fetal globin gene, which is normally turned off in adults, is currently turned on, at least partially, in patients with sickle cell disease using a drug called hydroxyurea. This reduces the frequency of sickle cell crises in such patients by 50 percent.

If we could more efficiently reprogram expression of the globin gene in question, we could have yet more beneficial effects in such patients. But, there are many other situations in which the principles of turning genes on and off may have beneficial effects for patients-- in the generation of completely compatible bone marrow; in the generation of skin cells that would not be rejected in bone patients, burn patients; in the generation of nerve cells in patients who have degenerative neurological disorders.

The final and sixth area is the one that has attracted the great majority of public attention, even though I would contend that the five I have listed so far are the ones that are of major interest to scientists; and, that is the creation of mature human clones. Now, from everything that you have heard so far, it does seem that this is a possibility although, to my knowledge and to the knowledge of my colleagues here, that has never been successfully attempted.

To do--to make human clones for scientific purposes, to me, is an offensive idea, one that is not scientifically necessary. After all, we already have spontaneously occurring identical twins, reared apart, reared together.

We have animals in whom the questions of interest can be answered. We have cultured cells in which many of the experiments of interest can be carried out.

There is, however, the issue of creating human clones to combat reproductive deficiencies. My own sense is that, if ever to be used, would be used incredibly sparingly.

We prize ourselves as human beings because of our diversity. And, diversity is the product of the mating of sperm and egg.

But, I think in our--in the early stages of this discussion, we need to contemplate whether there might be any rare situations in which it might, indeed, be acceptable to contemplate human cloning under strict conditions of guidance. It's for that reason that I particularly applaud the President's decision to refer the issues of human cloning to the National Bioethics Advisory Commission, which you will hear more about in a moment from Dr. Murray.

As you know, research on human embryos has been restricted in many ways through the NIH. About two and a half years ago, a panel that I commissioned under the leadership of Dr. Steven Meuller, previously the president of Johns Hopkins, reviewed all forms of human embryo research and recommended to the NIH that some be considered for funding, others not and others reserved for further deliberation.

Among those which they recommended not receive federal funding was the cloning of human beings in the manner described here. And, I agree with that conclusion.

In addition, we had a presidential order imposed in December of 1994 and amendments to our appropriation bills in the last 2 years that would forbid any experiments that would lead to the cloning of human beings.

As has been said repeatedly now, the President yesterday directed both a government-wide restriction on the use of federal funds for human cloning, extending the ban beyond research and beyond the confines of the Department of Health and Human Services and also asked for a voluntary moratorium in the private sector on human cloning experiments until the Commission has carried out its work. And, again, I applaud the decision to calm the public and reassure them that such work is not going on in the United States to allow the Commission to do its work and for the public to debate these important issues.

And, in that vein, I welcome the opportunity to have spoken to you today and to air these issues further with you. Thank you.