

Cloning and Genetics: The Brave New World Closes In

Is Dolly Really a Clone?

When the creation of Dolly, the first mammal cloned from adult cells, was first announced in February of 1997 there was a storm of publicity and controversy. While many wondered about the purpose of animal cloning and the possibilities such a success held for further animal applications, others were more concerned about the possible application to human beings. If we can clone sheep, can we clone humans? Should we clone humans? Why should we clone humans? Should humans be cloned to provide a baby for childless, infertile couples? Should we clone humans for embryo research? Should we clone humans to make extra copies of people with good genes? Would clones have a soul? While I answered these and other questions about human cloning in my article *Can Humans Be Cloned Like Sheep?* in retrospect, there was one question that was virtually ignored at the outset: Was Dolly a true clone?

Looking back, this appears to be a legitimate question that should have been more obvious. After all, Dolly was the only success amid 276 failures. There were 277 cell fusions made, with only 29 growing as embryos. All 29 were implanted into 13 ewes with only one pregnancy and one live birth. Dolly really beat the odds. There was also the fact that Dolly was not cloned from a currently living adult. Dolly's older twin had been dead for several years. Some of her tissues were harvested and kept frozen in the lab, so there was no live animal with which to compare Dolly.

Dolly's authenticity was formally challenged in a January 30, 1998 letter to the editor of the journal *Science*{1}. The authors offered seven reasons for skepticism concerning Dolly's identity as a clone of an adult cell. Among them was the fact that Dolly was alone and not yet joined by another adult clone from the Roslin Institute or any other laboratory. Also, though omitted by the original paper, it had been learned that the original sheep had been pregnant when the tissues were removed, raising the possibility that Dolly was cloned from a fetal cell rather than an adult cell. In addition, the questioning scientists called for additional genetic tests to establish Dolly's identity.

Although Ian Wilmut, the Scottish scientist who is Dolly's co-creator, admitted that Dolly might be a one in a million fluke, he and others were busy performing genetic tests to fully establish that Dolly was an authentic clone from an adult cell. Other labs had so far failed to duplicate Wilmut's success after hundreds of tries. This may not be so unusual since Dolly was the only success out of 300 nuclear transfers and the real odds may be as high as one in 1000. There was no way to know for sure. Wilmut may have gotten lucky indeed to achieve success after only 300 tries.{2}

A pair of papers in the British journal *Nature*{3} remedied much of the concern over Dolly's authenticity. DNA microsatellite and DNA fingerprinting analyses conclusively demonstrated that Dolly was an identical DNA copy of the cells of a 6-year-old ewe and not a clone of the fetus carried inside that ewe.

Cloning Mice Makes Cloning Humans More Feasible

Even with the clear success of cloning sheep, which Dolly's appearance and confirmation make plain, many doubted that the technology used to produce Dolly could be applied to humans. This skepticism was largely due to the universal failure to clone mice from adult cells.

Mice have a number of advantages as experimental animals for cloning. The gestational time in mice is very short—a matter of weeks, their embryos are easier to manipulate than sheep and cows, and their genetics are already well understood.^{4} But it was widely recognized that the early development of mice and sheep is significantly different. In sheep, the DNA in the newly formed nucleus remains dormant for several days. This was suspected to provide time for the DNA to be reprogrammed from its original function to embryonic functions. Mice, on the other hand, begin using the DNA in the newly formed nucleus after just 24 hours. It was thought that this might prove to be insufficient time for the DNA to be reprogrammed.

However, this too has been overcome, and in dramatic fashion. In July of 1998, *Nature* published results by T. Wakayama, working in Hawaii, documenting the cloning of mice.^{5} And not just one mouse, but over 50 mice. Three successive generations were cloned, raising the conundrum that the “grandmother” was the twin sister of the “granddaughters.”^{6}

But what did Wakayama and his colleagues do that was different to bring about success? Strangely enough, no one is really sure. Apart from a few tricks of timing, the major difference seems to be that they used a cell type that no one had used before, and it worked! As an aside, Wakayama tried other adult mouse cells (neurons and testicular cells) that only brought about the usual negative results.

But they also tried cumulus cells. Cumulus cells are a non-growing group of cells that surround an egg cell after it is released from the ovaries. This served to confirm the suspicion that adult cells need to be quiescent, or non-growing, to be successful in cloning experiments. Still, the nuclear transfer technique employed by Wakayama was successful between 2 and 3% of the time using cumulus cells. This rate of success is ten times better than the technique that led to Dolly, but still very low, making the process tedious.

The success with cumulus cells is why the first cloned mouse was named Cumulina. It is also interesting that only cells from females have been successful in cloning attempts thus far. This could be problematic. For, you see, if all you need is a quiescent adult cell, an egg, and a womb, well, male involvement isn't really necessary. Perhaps it's best not to speculate what, if anything, this may mean in the future.

For many, the real significance of successful mouse cloning techniques is its application to humans. The early stages of embryonic development are very similar in mice and humans. Therefore, many believed that since cloning mice seemed next to impossible because of the early onset of DNA activity in mice and humans, cloning humans would also remain technologically impossible. Cumulina and her sisters have changed all that.

What Will Animal Cloning Be Used For?

So now we can clone sheep and mice. Apart from the possibilities for humans, what's the big deal? Why are scientists and pharmaceutical companies spending so much time and money trying to clone animals? Quite simply, the combination of the possible relief of human suffering from genetic disease with the potential to turn a handsome profit makes animal cloning nearly irresistible.

In the December 1998 issue of *Scientific American*, Ian Wilmut spells out some of the potential uses of animal cloning.^{7} Principally, cloning will be used to create large numbers of what are called transgenic animals. Transgenic animals are genetically engineered to contain genes from another species. Wilmut and his colleagues created Dolly in an attempt to discover a more reliable method of reproducing transgenic sheep.

Creating transgenic animals is very tedious, difficult, and risky work. The Roslin Institute and PPL Therapeutics, for whom Wilmut works, transferred into sheep the gene for human factor IX, a blood-clotting protein used to treat hemophilia. With the proper genetic enhancement, sheep will produce this blood-clotting factor in their milk, which can then be harvested and sold on the market. The first transgenic sheep produced this way, Polly, was born in the summer of 1997. It is actually simpler to clone Polly than it would be to create another transgenic sheep through gene transfer.

Cloning offers many other possibilities for reproducing other kinds of transgenic animals. One is the production of animals containing transgenic organs suitable for organ transplants into humans. Pig organs are just about the right size for transplantation into humans. However, a pig heart, or liver, or kidney, would be severely and quickly rejected by our immune system. However, if the right human genes could be transferred into pigs, the organs they produce would be recognized as a human organ and not a pig organ. There would still be the problems associated with any organ transplant between humans, but these are much more manageable than cross-species immune rejection. At present, thousands die every year waiting for organs to become available. Cloning such transgenic animals could create a large and renewable source of organs for transplant.

Transgenic animals could also be created for research purposes to study human genetic diseases. Transferring defective human genes into appropriate animal hosts could produce more workable research vehicles for discovering new treatments and cures not possible using human subjects. Cloning of transgenic animals may also prove useful to create cells helpful in treating human diseases such as Parkinson's disease, diabetes, and muscular dystrophy. In addition, cloning could be used to produce highly productive herds of sheep, cows, and pigs from animals that are already known to be excellent milk, meat, and leather producers.

Obviously, the uses of animal cloning seem limited only by our imaginations. Of course, if you are already opposed to the use of animals in experiments, or even in their use for food, these ideas are fraught with ethical difficulties. As a Christian, however, I have answered this question. The Lord Himself produced the first skins for humans in Genesis 3:21 and later after the flood, the Lord allowed animals to be used for food (Gen. 9:2-4). While the utmost of care needs to be given to ensure that God's creatures, for whom we have been given responsibility (Gen. 1:26-28), do not suffer needlessly, the Lord clearly allows animals to be used to enhance our own lives, even if it costs them theirs.

New Uses for Human Embryo Research?

What if I told you that recent breakthroughs in human genetic research might make it possible to dramatically treat patients with Alzheimer's, Parkinson's, heart disease, diabetes, spinal cord injury, and a host of other degenerative diseases? In some cases, these treatments may actually cure many of these diseases and would not require the use of cells obtained from aborted fetuses. Hopefully, I've got your attention.

The November 6, 1998 issue of Science^{9} announced the first successful attempts to cultivate human embryonic stem cells that have the potential to treat all the above diseases and more. However, they come with their own set of difficult and perhaps more serious ethical concerns.

First, just what are embryonic stem cells? Stems from plant seedlings give rise to all sorts of different structures such as trunks, branches, leaves, flowers, and eventually seeds and fruits. Animal embryonic stem cells do much the same thing. Stem cells have the potential to grow into just about any tissue that is present in the adult organism. Researchers call this potential totipotency, meaning they are potent to produce all tissues. Embryonic stem cells have been isolated from mice since the early '80s. Such research has been impossible in humans for ethical reasons. Stem cells

only come from embryos in the earliest stages of development.

No one was willing to simply use embryos to obtain stem cells, thus killing the embryo, every time stem cells were needed. But, if stem cells could be isolated and cultivated in the laboratory so they could grow and divide and maintain their stem cell functions, then a continual supply could be maintained without risk to further embryos. What is called a stem cell line would effectively be created that could be used indefinitely. This research was greeted with such comments as "extremely important," "very encouraging," and "a major technical achievement with great importance for human biology." {10}

What you may have noted in the above description is that a human embryo must still be used to create this stem cell line. In fact, the study reported in Science indicates that thirty-six embryos obtained from in vitro fertilization clinics in Madison, Wisconsin and Israel were used to create five stem cell lines. The embryos were obtained with the consent of the individuals whose eggs and sperm were used to create them and the approval of the local institutional review board.

The major concern expressed so far is for the legality for other labs to use these cells. Since there is a ban on the use of federal funds for research involving tissues derived from human embryos, this research was carried out using private funds from Geron Corporation, a Menlo Park, California biotechnology firm. The availability of these stem cell lines now raises the question of whether these cells can be used by other labs currently funded by government grants. Predictably, one researcher is applying for grant money to use these stem cells to deliberately test, and hopefully repeal this restriction. {11}

Proponents of stem cell research criticize the federal ban by suggesting that this leaves the government out of the regulatory picture since no guidelines have been issued for private research. I agree that the lack of guidelines for private industry is an oversight, but opening up government funding is not the answer. The ban should remain in force. Guidelines need to be issued that forbid this important work as long as human embryos are sacrificed to produce these cell lines. Research in animals should be encouraged to see if stem cells could be produced by other means. The end does not justify the means.

The Prospects for Human Cloning: The Enigma of Dr. Richard Seed

I am frequently asked how soon I think the first human clone will be produced. I usually respond that somewhere in the world within the next five to ten years, someone will announce the creation of the first human clone. But if we are to believe Dr. Richard Seed, the first human clone will appear before the year 2001. In December 1997, Dr. Richard Seed, physicist turned fertility specialist, announced that he intends to clone human beings. He said, "I know of at least fifteen people who want to clone humans, but haven't got quite up the nerve to do it." {12} When asked if he had the nerve, Seed replied, "I have the nerve."

Richard Seed appeared in the news again in September of 1998 when he announced his plans to clone himself in two years and that his wife agreed to carry the baby! {13} Seed reported that he had received hundreds of calls from individuals that want either themselves or their dying children cloned. Seed thinks this is a first step to human immortality. On January 7, 1998 Seed affirmed on ABC News Nightline his remarks from a National Public Radio interview, that cloning technology will allow us to "become one with God. We are going to have almost as much knowledge and almost as much power as God." {14}

Right now you're probably thinking this guy is a kook. Why worry about him? Well, that's precisely why we need to pay attention to him. He has the ability; he perfected embryo transfers in humans.

He certainly has the motivation and nerve, and he is still seeking the cash to carry it out. But if he is accurate in the number of calls he has received, money may not be a problem for long. And even if the U.S. Congress passes a bill banning human cloning, Seed has said he will move his operation to Tijuana, Mexico.

People like Richard Seed fully explain why I believe someone, somewhere in the world will produce a human clone very soon. The question is, Are we going to just throw up our hands and surrender, or will we continue to stand up for the sanctity of human life and the sacredness of the human embryo?

If we don't think this through carefully and organize a cogent response to this threat to human dignity, the attitude of people like Prof. James Robl at the University of Massachusetts at Amherst will prevail. He said:

There is no clear-cut definition for what is life. And this is something, I think, that society is going to have to think about, is going to have to make some definitions, and those definitions may not be permanent, they may change as new technologies are developed. There is a fine line, and the line, at the early stages, is really based on your intentions of what they are to be used for as opposed to necessarily what they are. So the question of what is life seems to change, I think, in people's minds based on what their concerns are or their own interests are in how we might use whatever it is we are producing. {15}

What Professor Robl calls for is an entirely utilitarian ethic. We define life, he says, based solely on what new technologies we develop. If a new technology, such as cloning or human stem cell production from human embryos becomes available, yet this technology threatens human dignity, we simply redefine human life to encompass the new technology. This is the frightening specter of a brave new world. We must oppose it and we must articulate why.

Notes

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