In our own image? Ethics and human cloning

By Anthony J. Zuccarelli and Gerald R. Winslow

The brave new world of cloning has opened uncharted territory. How should thoughtful Christians relate to its ethical implications?

Cumulina! Not a romantic town in a faraway island. Not an exotic dish. Not anything you could ever have guessed a few months ago. Though Cumulina is only a mouse, she is a brave new entrant into a brave new world. Nested in wood shavings in clear plastic cages in Honolulu at the University of Hawaii, Cumulina and about 50 other mice are the latest pioneers in a scientific quest with frightening implications. The mice look quite ordinary, indistinguishable from any at an animal facility. However, the group is unique because they have only female "parents." Like Dolly, the best-known sheep since "Mary's Little Lamb," the mice were produced by somatic cell nuclear transplantation—in other words, by cloning.

Dolly ignited a firestorm of debate. The announcement of her birth by Scottish scientist Ian Wilmut in February 1997 [1]* raised the prospect that, in the near future, it may be possible to clone human beings. The philosophical and ethical implications occupied the news media for months and put human cloning on the agenda for legislative bodies and think-tanks around the world. For a year and a half, the debate continued, restrained only by the inability of other scientists to repeat the process, by doubts that the technology could be adapted to humans, and by suggestions that Dolly's conception may not have been immaculate.

Those firebreaks were removed by three reports in the July 1998 issue of the journal *Nature*. Two groups provided convincing evidence that Dolly is genetically identical to the ewe from which she was derived; she is indeed an authentic clone [2,3]. The Honolulu group showed that somatic cell nuclear transplantation can be repeated, creating three successive generations of mouse clones [4]. They also provided evidence that this can be done with species thought to be difficult to clone, including humans. According to the editor, "it becomes all the more probable that, where someone is legally allowed to [clone humans], they will." [5] That probability took substance as physicist Richard Seed announced that he has identified clients, financial support, and scientists to staff his proposed Chicago cloning clinic.

Should humans be cloned?

But, should humans be cloned? As Adventist Christians, with an appreciation of the value God places on human life and our responsibilities as stewards of the earth, the matter needs to be carefully examined. After exploring the science and economics of cloning, the objective of this article is to identify ethical principles that might guide us through the web of issues and emotions surrounding the prospect of asexual human duplication.

Let's begin with sexual reproduction. Your biology textbook says that when two germ cells unite to fertilize, they combine their genes to create a single-celled zygote. The genetic material of the zygote, in the form of DNA, is later replicated and distributed equally to two daughter cells, forming the two-celled embryo. The embryo develops by ordered cycles of DNA replication and cell division. Every cell receives a complete copy of the genetic material, half originally provided by each parent. When the embryo reaches a critical

number of cells, they begin to specialize by selectively expressing some genes and turning off others according to a built-in program. Depending upon the pattern of expression, some will become nerve cells, others muscle cells, and still others skin cells. Continued differentiation eventually forms a fetus with hundreds of specialized cell types that will make up the newborn organism at birth.

Though sexual reproduction is a common theme, it is not universal. Your biology textbook also describes single-celled microorganisms, like bacteria and yeast, whose regular mode of reproduction is asexual. They simply divide into two genetically identical cells, clones of each other and of the parent cell. Many plants also reproduce asexually. A fragment scattered by a neighbor's lawn mower can start a growth of crab grass in your lawn. A favorite grapevine, rose bush or house plant can be cloned by rooting a cutting until it grows into a complete plant. Some animals, like starfish and earthworms, can also regenerate from a fragment. Each of these cases of asexual reproduction depends upon the fact that every cell in a complex organism carries all the genes of the entire organism, even if the cell came from the leaf of a plant where it used only the genes needed for "leafiness."

Genes turned off during embryonic development were thought to be permanently inactivated in animals. Decades of failed attempts to generate whole animals from isolated body cells (called somatic cells) established the belief that they were terminally differentiated. There seemed to be no simple way to flip their genetic switches back to the "start" position—until Dolly.

Somatic cell nuclear transplantation

Following the lead of experiments performed in the 1950s and 1960s, Dr. Wilmut obtained sheep oocytes (eggs before maturation) and manually removed their nuclei (which contain the genetic material) using fine glass pipettes. Then he fused the gene-less oocytes with somatic cells taken from the udder of an adult ewe. The nucleus of the udder cell replaced the genes normally supplied by the sperm and egg at fertilization. Oocyte cytoplasm apparently provided the proper environment to reset the genes in the udder nucleus, allowing them to be expressed in the normal sequence for embryonic development. After a period of growth in nutrient solution, the reconstituted oocyte, which had become a multicellular embryo, was implanted in an ewe for full-term development [1].

That's how Dolly came to be. The crucial steps in the process are reflected in its name—somatic cell nuclear transplantation. With several modifications, the Honolulu team used the procedure to make Cumulina, the first cloned mouse, and clones from the clones in two succeeding generations [4].

Several facts are worth emphasizing. Dolly and Cumulina have neither fathers nor mothers in the conventional sense—parents who contributed germ cells to their conception. Rather, each has a nuclear donor who provided all the nuclear genetic material, an oocyte donor who provided the cellular "incubator" into which the genes were placed, and a gestational parent who nurtured the embryo until birth. Since none of the participants were male, one might say that Dolly and Cumulina each have three "mothers."

Second, a clone has the same chromosomal material as its nuclear donor. Some have likened a clone to a delayed identical twin of the nuclear donor. The oocyte donor contributes a minuscule amount of genetic material found in its mitochondria; the gestational parent provides only a nurturing womb. Dolly's three parents were Finn Dorset, Poll Dorset, and Scottish Blackface sheep, respectively. She looks just like her Finn Dorset nuclear "mom."

Third, though cloning is an amazing achievement, it is dauntingly inefficient. More than 400 sheep ova were used to produce Dolly [1]. All the others died at various stages. Cumulina and her cohort represent about 2.5 percent of the attempts in the Honolulu experiments [4]. Obviously, sexual reproduction is more efficient, simpler, and usually more satisfying.

That may provoke the question, "Why attempt cloning at all?" Surprisingly, the primary motivation is to duplicate animals, not humans. The value of cloning is the consequence of a crucial difference between sexual and asexual reproduction. Consider the uncertainties of conventional animal breeding. Calves born to a champion milk producer, for instance, would get only half of their mother's genes. Since milk production depends on many interacting genes, few of her offspring are likely to inherit the precise combination that made her such a great milk cow. After winning the Triple Crown, for example, Secretariat sired more than 400 foals borne by the best mares in the world. Not one of them had a successful racing career! Sexual reproduction limits how much you can stack the deck in favor of desirable traits.

Transgenic animal factories

Clones, in contrast, have exactly the same genes as their nuclear donor. Cloning would assure that the genetic makeup of sheep with particularly thick, soft fleece or chickens that lay lots of low-cholesterol eggs would be precisely replicated. Though such traits are desirable, others are still more highly prized. The engine driving development in nuclear transplantation is the desire to produce animals that carry human genes, so-called transgenic animals.

During the past 25 years, biotechnologists have identified and isolated human genes that code for various cellular components and products. As a practical result, insulin and other simple human proteins are now made by genetically engineered bacteria growing in

vats of broth. Many valuable proteins, however, are too complex for bacteria to replicate properly. One alternative is to use cultures of genetically modified human or mammalian cells, but growing them is expensive and they make only a small amount of the desired product. The oldest method, extracting proteins directly from cadavers or outdated human blood, is avoided because of the risk of contamination with infectious agents like HIV or hepatitis viruses.

Pursuing cost efficiency and safety, biotechnology has shifted to domesticated animals that make products under the direction of human genes added to their chromosomes. In the best cases, the added DNA directs the animal to secrete large quantities of human protein into its milk. Cleverly called pharming, the first wave of transgenic animals is represented by goats, cows, pigs, and sheep in the U.S., Scotland, and the Netherlands that make such proteins as antithrombin II (an anti-clotting agent), alpha-1-antitrypsin (absent in emphysemics and useful in treating cystic fibrosis), blood clotting factors (absent in hemophiliacs) and interferons (antiviral agents). Having farm animals convert grass into proteins is like having a goose that lays golden eggs—maybe better! Some therapeutic proteins are worth many times their weight in gold.

OK, so animals that secrete useful human proteins are valuable. How does cloning enter the picture? High-yield transgenic animals are difficult to make; cloning may make it easier. The first step in making a transgenic animal is to identify and isolate the human gene for the desired product—say, an antiviral protein. Next, the gene is joined to a DNA segment that controls when and where the gene will be active. A typical strategy is to use a segment that directs the gene to make its antiviral protein in the milk-producing cells of the mammary gland. These steps are readily accomplished using tried-and-true molecular genetic techniques, but subsequent stages are technically demanding and inefficient. Several hundred copies of the gene-plus-controller DNA are laboriously microinjected into fertilized oocytes. Zygotes that develop are later implanted in surrogate mothers for gestation. The efficiency is disappointingly low—typically, less than 0.5% survive to birth and test positive for the transgene. Even fewer secrete useful quantities of the protein in their milk. Clearly, it can take years to establish a productive transgenic herd.

Reliable methods for cloning would change the picture. As before, a human gene must be isolated and joined to a control segment. Then, instead of microinjection, gene-plus-controller DNA is simply added to the liquid in which cultured animal cells are growing. Under the right conditions they pick it up on their own or after a brief electric pulse. Using standard selection methods, cells that have accepted the transgene can be purified and tested to learn if they are likely to be good protein producers. Since these manipulations are done with cultured cells, rather than animals, they can be accomplished in a few days. Successfully modified cells would then be used to make whole animals by transferring their nuclei to enucleated oocytes.

Tissue for transplantation

A further role for cloning is the creation of animals with "humanized" tissues to meet the great need for transplant organs. Hyperacute rejection of animal organs is due to an arrangement of sugar subunits on the surfaces of the cells that is not tolerated by human recipients. Since it is possible to subtract as well as add genes, "knocking out" the genes responsible for the offending surface modifications would make animal organs more compatible with human hosts.

The mysterious ability of oocyte cytoplasm to reprogram a nucleus is intriguing. Some predict that it may be possible to take even greater advantage of this property. After a nucleus from a patient has been reset to an embryonic state within an oocyte, it may be possible to instruct it to replicate and mature into a different cell type. The aim would be to generate specialized tissues that could be used to treat a wide range of human diseases—young pancreatic islet cells to treat diabetes, skin cells to heal burns, nerve cells to repair spinal injuries or reverse Parkinson's disease. Since the transplanted tissue is derived from the patient, it would be perfectly compatible and would avoid immune rejection. Rather than consider the ghoulish possibility of cloning people to be used for "spare parts," nuclear transplantation might be able to reprogram human cells so that they will grow into isolated organs or organ-like tissues.

Cloning and ethical issues

Cloning technology promises awesome benefits, but at what cost? Some warn that it may be high—undermining human dignity and eroding family relationships. Let's examine these concerns thoughtfully to determine if they are useful guides in making decisions about cloning. We will organize our discussion around seven themes of Christian ethics: protection from harm, consequences for human freedom, effects on family structure, potential for relieving suffering, stewardship of personal resources, truthfulness, and the potential for understanding God's creation. [6]

1. Protection from harm. Dolly's creator, Ian Wilmut, identified the most compelling reason for not attempting to clone humans: it would result in the loss of countless human ova and in the deaths of many fetuses at various stages of development, including those near full-term. It also poses a high risk for malformed infants and infant deaths. In his early experiments, about 60 percent of cloned lambs died soon after birth and many showed physical abnormalities. Cloning is morally precarious because it is medically hazardous. The

standard of Scripture is to avoid putting human lives at undue risk of injury or death, especially the lives of the vulnerable. The same principle is reiterated in the physician's oath to "do no harm." It prohibits an undertaking that would result in dozens of stillborn, malformed, or unviable infants in order to produce a healthy child.

The National Bioethics Advisory Committee, appointed by the President of the United States, decided that human cloning is presently unacceptable for reasons of safety [7]. Their judgment was based on the state of a technology still less than two years old. They recommended a temporary moratorium, fully expecting further experience to improve the success rate. A permanent ban would be equivalent to prohibiting forever public air travel in the days immediately after the first successful, but death-defying, airplane flight at Kitty Hawk. Dolly and Cumulina represent mileposts in a long series of biological developments spanning five decades. The current pace of progress requires that we reassess the technology at intervals to determine if it has matured beyond the point of balancing benefits against risks.

2. Human freedom and dignity. Christians believe that humans have dignity because they were created in the image of God with autonomous "power to think and to do." The prospect of asexual human reproduction often evokes a contrary and disturbing vision—armies of soulless zombies marching in the genetic footsteps of their progenitors. Our fear of human carbon copies is powerful, almost visceral. It derives, in part, from our tendency to equate appearance with personal identity. Last year a newspaper featured the responses of teenagers to the prospect of human cloning. "So people will be cloned," said one 18-year-old, "but you won't know who the clones are...And how do you know if they're going to even have a soul? How do you know, like, what's walking down the street?"

By contrast, we have little difficulty accepting the fact that "identical" (monozygotic) twins are not really identical. They develop distinct personalities and temperaments as a consequence of their independent experiences, environments and choices. In spite of their identical genes they become fully unique "souls." A cloned person would mature into an individual who is entirely distinct from the nuclear donor for the same reasons but, in addition, the clone would have a different "mother," would grow up in a different family and would live at a different time than the donor. Consequently, the belief that clones of Albert Einstein or Michael Jordan would retrace the life histories of their progenitors is totally unfounded. Hasting Center bioethicist Erik Parens summarized the matter succinctly when he observed, "You can't clone a self." [8]

Though clones would be unique individuals, some may attempt to limit the expression of that uniqueness. Can you imagine the clone of a famous pianist being compelled to spend hours at the keyboard to the exclusion of other pursuits? Would some be inclined to produce clones for commercial purposes or sacrifice them for their organs? Our view is that it is morally indefensible to create clones to be used solely as sources of transplantable organs, for commercial exploitation, or as subservient tools. We should strongly oppose "commodification" and "genetic bondage" of human beings. Cloning, like all powerful technologies, can be a tool for good or for ill. Any use that would undermine or diminish the personal dignity or autonomy of human beings must be rejected.

3. Alleviating human suffering. Full, creative application of our minds and bodies to advance the healing ministry of Christ is a fundamental principle of Adventist theology, which expresses itself, in part, in our worldwide educational and medical programs. Implicit in the Great Commission is our responsibility to prevent and relieve suffering with the means at our disposal. Cloning may be a potent healing tool if it allows us to prevent the transmission of genetic diseases or to create replacement tissues and organs for repair or transplantation. Retaugh Dumas at the University of Michigan expressed an opinion that may strike a chord with those committed to the ministry of healing; "I could make a moral argument that if these techniques are available and we don't use them, we are letting society down." [9]

4. Safeguarding the family structure. During the announcement of a cloning moratorium, the U.S. President voiced the concern that it "has the potential to threaten the sacred family bonds." The image of infants mechanically produced outside the family circle is indeed unsettling. God's plan is for children to be nurtured within the context of a loving family with the presence, participation, and support of a father and a mother. Since nuclear transplantation can be used to achieve human reproduction when other methods are ineffective, it should be attempted only within the setting of a faithful marriage and in support of a stable family. For this reason, we should avoid the moral complications that would arise if a third party were to act as a gestational surrogate or be the source of the genetic material. [10] Cloning could be a valuable last resort for couples who wish to have children but are unable to produce functional germ cells. In such situations, nuclear transplantation would serve as an advanced form of assisted reproduction. Many have proposed the hypothetical case of a couple whose only child is dying and who want literally, to replace the child. Some would consider this an appropriate application for nuclear transplantation.

5. Wise use of resources. Given the technical challenges of cloning, it is expensive and will likely remain so for some time. An American couple, for example, has paid $2.3 million to Texas A&M University to clone their beloved dog Missy.

In free societies, people are at liberty to spend their money in a multitude of ways, including foolish ones. But Christians are called to use their resources in a manner that reflects responsible stewardship. This commitment means putting the kingdom of God first. And it means self-sacrificial attention to the needs of others. Thus, Christians should assess the expense and the value of cloning in light of faithful stewardship.

6. Truthfulness. Scripture teaches us to value honest communication and to refrain from lying. When new technologies, like cloning, are developed, it is not uncommon for some enthusiasts to overstate the benefits and underestimate the costs and risks. On the other hand, it is tempting for some naysayers to exaggerate the risks and misrepresent the goals. Christians have an obligation to understand and promote the truth.

7. Understanding God's creation. God intends for human beings to grow in their appreciation of His creation. Our desire to understand the human body and the mechanism of human development is no different from the drive to investigate other natural phenomena. Efforts to understand the world around and within us by ethical research, an impulse instilled by our Creator, should be encouraged and supported. For those who are sensitive to signs of God's hand in the physical world, such knowledge is evidence of His love and power.

Currently, there is widespread ethical agreement that human cloning should not be attempted. Proponents appear to be few. Safety concerns alone should be sufficient to rule out applications to humans at this time. But as reproductive biologists accumulate more experience with animal cloning, the procedure will become more efficient and cheaper. Attempts to clone humans can then be expected.

Christians have an opportunity now to reflect on the ethical issues that human cloning presents and to consider them in the context of abiding biblical principles [6]. To do this ahead of time is an act of faith and of moral maturity.

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