

Reproductive Cloning

By Richard Mollard

The procedure:

In reproductive cloning, the DNA of an unfertilized egg is removed and replaced by donor DNA, obtained from cells from another individual. The egg is then coaxed into believing that it has been fertilized and starts dividing, to generate new cells (and form an embryo) in a laboratory culture. Up to this point, the procedure is similar to therapeutic cloning. Once the egg has divided sufficiently, the resulting embryo is then implanted into the uterus of a surrogate mother, where it can develop until birth. In contrast to natural reproduction, reproductive cloning does not create a genetically new and unique individual through the recombination of each chromosome set from each parent. Instead, only the DNA from the DNA donor is present, which makes the newborn a genetic replicate of the DNA donor, a clone.

High failure rates:

While this procedure may sound relatively easy, reproductive cloning is fraught with profound technical and biological problems. The birth of normal animal clones is very rare. Despite cloning and implantation of hundreds of embryos, very few live cloned animals have been obtained thus far, around 1 percent of all the eggs that received donor DNA.

In addition, the clones that do survive are in very poor health with many problems, including obesity, arthritis, infection, breathing problems and death at young ages. At this stage, it is not



Clone #1: Dolly the sheep, was born to stardom on July 5, 1996. After a short life of six years (sheep live up to 12 years) Dolly had to be euthanized on Feb. 14, 2003, because of progressive lung disease. Subsequent post-mortem examination confirmed a virus-induced lung tumor. (Image kindly provided by the Roslin Institute, Edinburgh, UK.)

known why the technique of reproductive cloning is so inefficient or why there are so many health problems in the few surviving clones. Scientists are actively working in this area and possible reasons are beginning to emerge.

Emerging concepts:

Every cell of the body contains exactly the same set of genes. The sum of these genes is known as the genome. Certain parts of the genome, i.e. certain genes, are either turned on or off during development, which allows a cell to become specialized as a brain cell or a heart cell, or any other cell type in the body.

Normally, genes that are crucial to orchestrated embryonic development are turned off, and remain that way, after the embryonic stage is over, for the rest of the life of the individual.

This process is regulated by mechanisms called epigenetic control of gene expression, where these genes become inaccessible in the genome for the rest of the life of the cell, and this state is even handed down to the cell's progeny, when the cell divides.

During reproductive cloning, the donor DNA that is introduced into the egg is "reprogrammed" by the egg, which turns some of the embryonic genes back on and others off, as appropriate in an egg cell at that stage of development. However, the donor DNA is obtained from the cell of an adult and is "old." Important embryonic genes have been silenced in the past of the "old" DNA, and are maintained that way. The smooth and orchestrated embryonic ballet of turning genes on and off therefore cannot take place, resulting in extremely high rates of pre-term abortions, miscarriages and birth defects.

Outlook for humans:

Human reproductive cloning at this stage is considered unsafe because there is no reason whatsoever to assume that cloning of humans

would be more efficient or result in fewer health problems or deaths than has been seen for reproductive animal cloning.

There are also significant risks for the mother, associated with carrying a grossly overweight fetus and having an abnormal pregnancy. Cloned newborn animals are often significantly overweight as compared to normal pups and have a large and dysfunctional placenta (this is often referred to as "Large Offspring Syndrome"). Reproductive cloning is, therefore, opposed adamantly by a vast majority of scientists, doctors and the general public at large.

Richard Mollard, Ph.D., is an embryonic stem cell specialist at the Institute of Reproduction and Development at the Monash University in Australia.