REPRO TRACKS

by Cliff Lamb, Texas A&M University

Somatic Cell Nuclear Transfer in Beef Cattle

The current status of cloning in the industry.

I was fortunate enough to have a discussion with a recent graduate student who indicated they would like to conduct a review of the status of somatic cell nuclear transfer (cloning). I realized in the nine years I have been contributing to the "Repro Tracks" column, I had not ever fully discussed the process in detail. Therefore, the focus of this article is to discuss the current status of somatic cell nuclear transfer in cattle.

Walt Disney expressed, "We keep moving forward, opening new doors and doing new things because we're curious, and curiosity keeps leading us down new paths."

There is not a better way to describe the progress made in the science of cloning. Cloning is a term well-known to the public. However, this is the term that has been used to describe the nuclear transfer process in mammals. Using the term "cloning" has caused a misunderstanding that offspring are produced to be both genetically and phenotypically the same as the donor, resulting in an exact copy of the original animal both in genetic coding and in appearance.

In reality, offspring produced through nuclear transfer are genetically identical to their donor but may not be identical phenotypically. For example, they may express different coat colors and patterns.

Cloning mammals

The first efforts in cloning mammals allowed for improvements in the techniques used to handle the fragile oocytes and permitted successful *in vitro* cultures before implantation. The first success in mammalian clones was three lambs created from enucleated oocytes that were fused to a blastomere from embryos at the 8-16 stage, followed by calves produced from a similar process, but with embryos at the 4-15 cell stage. These successes caused researchers to ask whether an adult cell nucleus could be cloned.

The success resulted in the creation of Dolly the sheep, who was cloned from an adult mammary gland tissue cell via somatic cell nuclear transfer (or cloning). Dolly was a tremendous scientific breakthrough as the first cloned mammal from an adult somatic cell to not only mature but to later produce offspring.

Somatic cell nuclear transfer, or somatic cell cloning, has become frequently used to produce transgenic cloned livestock through reprogramming of cells, forcing the cells to lose their lineage-specific epigenetic marks and return to a state of totipotency (the ability of a cell to give rise to unlike cells and so to develop a new organism or part).

However, cloning remains limited in its use due to the low success rate of producing viable, adult offspring. Low efficiency of cloning has been associated with alterations in placenta formation, aberrant reprogramming of the somatic cell donor nucleus, atypical oocyte activation and even culture conditions for the reconstructed embryos.

Cloning and cattle

Studies utilizing cattle have helped pave the way for an improved nuclear transfer process by attempting to solve the crucial problems facing the efficiency of cloning.

Few studies have been done on the effects of different culture media on cloning embryos, presumably due to the early assumption these embryos would behave similarly to embryos produced by *in vitro* fertilization under the same culture conditions, but cloned embryos have different culture requirements. In a natural setting, embryos move from the oviduct to the uterus where the secretions and gas atmosphere differ in composition. Therefore, the culture system should reflect this

two-step process (beginning with one type of culture medium then adding ingredients later for the second step) to mimic the physiological conditions. Serum starvation in the medium induces features of an unrestricted epigenome that correlates with a long-term increase in donor cell plasticity and cloning efficiency. However, the addition of serum in the second part of the two-step system not only improves the development rate producing a greater number of blastocysts, but also improves the quality of these embryos without greatly affecting the gene expression patterns.

The differential gene expression pattern that has been observed in cloned embryos cultured in different media confirms the feasibility that the quality of the embryos can be manipulated by the use of chemically defined media, favoring the two-step process that mimics natural conditions.

Cloning is a technique that is still in its infancy despite having years of research contributing to its discovery and efforts to advance it. One reason for this is that no solution has been able to overcome the cellular damage that occurs during the process.

Unfortunately, at the current rate it takes to clone an animal, unfavorable genetics can often be bred out of cattle rather than cloning a desirable stud. However, cloning provides significant opportunities to preserve desirable genetics or to provide a potential solution to the growing organ shortage in the biomedical field, as well as cures for medical diseases, such as diabetes.

Nonetheless, all advanced reproductive and genetic technologies could have a place in the future of beef cattle production. Determining the best opportunities likely depends on the cost and value of the desired offspring. AJ

Editor's note: Cliff Lamb is the animal science department head and a professor at Texas A&M University in College Station, Texas.