Researcher explores the current state of domestic animal cloning

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Researchers are able to clone domestic animals using various techniques, including embryo splitting and nuclear transfer, but the expense and inherent inefficiencies of most cloning processes have limited procedures to research and certain agricultural activities. Carol L. Keefer of the Department of Animal and Avian Sciences of the University of Maryland has contributed a paper to the *Proceedings of the National Academy of Sciences* that provides a contextual overview of the innovations and contributions of cloning while seeking to answer an important question: If cloning is impractical and inefficient as a means of producing animals, and in the absence of societal acceptance for transgenic products, how is artificial cloning being used?

Somatic cell nuclear transfer (SCNT) involves the implantation of a donor nucleus into an enucleated oocyte to produce a viable embryo. It was through SCNT techniques that Dolly the sheep was cloned in 1996. That accomplishment shook the foundations of genetic science, but it also highlighted the major inefficiency of SCNT, as Dolly was the only live offspring resulting from 29 transferred embryos. Multiple barriers to artificial cloning, including epigenetic changes that occur during development that researchers are only beginning to understand, prevent its viability for the efficient production of domestic animals.

While the concept of artificial cloning evokes images of identical, factory-produced animals, such science fiction ideas are still wildly beyond the means of researchers. Artificial cloning has instead been used to reproduce breeding stock from animals with advantageous genotypes and to produce fertile clones from sterile animals. Keefer points out that in Texas, beef cattle have been "resurrected" based on their carcass traits. But the mass production of domestic animals is inhibited by a number of developmental genetic hurdles, and only an estimated five to 15 percent of transferred embryos actually result in live offspring.

However, SCNT techniques are quite advantageous for the production of transgenic animals. Multiple methods are used to produce transgenic mice expressing desired traits for scientific research. Transgenic cattle, sheep, and pigs have been produced expressing desirable industrial proteins like spider silk, and increased nutrients in milk. Keefer also cites a study in which the prion protein that causes mad cow disease was knocked out in transgenic cattle using SCNT.

Yet, only a single product from a transgenic animal has been approved for sale in the United States—the biotherapeutic protein antithrombin. "Whether transgenic animals ever fulfill the animal production-related promise researchers envisaged will depend on societal acceptance and revised regulatory guidelines," Keefer writes. Instead, the chief value derived from transgenic animals is in scientific research, including such developments as cloned pigs that have served as controls and recipients for neural stem cells in work toward

spinal cord repair.

Because SCNT is so inefficient, much research has been devoted to improving techniques, and the result has been a number of answers to basic questions in developmental and reproductive biology. For instance, SCNT was used to determine the role of foreign paternal antigens in the establishment and maintenance of pregnancy—researchers demonstrated that a mare could carry to term a pregnancy initiated by her identical clone, implying that foreign paternal antigens are not necessary for establishing such a viable pregnancy.

Noting the value of SCNT research for answering basic science questions, Keefer concludes, "Future studies taking advantage of such unique research opportunities provided by SCNT may help answer questions and solve technical issues in reproductive medicine and regenerative studies."

More information: "Artificial cloning of domestic animals." *PNAS* 2015 112 (29) 8874-8878; published ahead of print July 21, 2015, doi:10.1073/pnas.1501718112