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Pfizer Animal Health Gift

Improving Survival Rate of Cloned Mouse Embryos

by Steve Bradt

Scientists at the School have found a novel way to boost the paltry survival rate of cloned mammals: When two genetically identical cloned mouse embryos are combined, the aggregate embryo is considerably more likely to survive to birth.

The team reported the results in the October 1 issue of the *European Molecular Biology Organization Journal.*

"At the blastocyst stage, an early embryonic stage just prior to implantation, mouse clones typically have a much lower than normal number of cells," says corresponding author **K. John McLaughlin**, Ph.D., assistant professor of Reproductive Physiology. "When we combined two clones at the four-cell stage, the embryos showed a remarkable improvement in viability, much greater than expected from the sum of their parts."

Despite the successful cloning of sheep, pigs, cats, and most recently rats, mammalian cloning—in which an ordinary cell's nucleus is transferred to an egg whose nucleus has been removed—remains remarkably inefficient. Of every 100 cloned mice, roughly one survives to birth.

The researchers found that when the clone hybrids were transferred back into the uteri of recipient mice, the survival rate jumped to 8 percent. The researchers even produced a litter of four cloned mouse pups, in stark contrast to the typical single pup born.

Cloning requires the precise genetic reprogramming of the nucleus inserted into an enucleated egg. This nucleus must abandon its former genetic program and adopt the genetic profile of an embryonic nucleus; failure to do so dooms the embryo.

"The paper provides a new insight into reprogramming following nuclear transfer," says Davor Solter, a developmental biologist at the Max-Planck Institute of Immunobiology who was not involved in this work. "It confirms indirectly that every cloned embryo is actually different and that reprogramming is random. It seems that two embryos that are epigenetically different can positively interact and complement each other, leading to correct temporal and spatial gene expression. That this type of interaction can take place was not obvious and it could only be demonstrated by the described approach."

McLaughlin and his colleagues are not yet sure why the aggregation of cloned embryos boosts survival, although one theory is that the combination of two embryos helps compensate for genetic deficiencies in either.

"The genetic reprogramming of a cloned embryo never seems to occur with 100 percent accuracy," McLaughlin says. "However, the group of genes that fails to reset properly differs in each individual embryo, meaning that each embryo that contributes to an aggregate can help mask the shortcomings of the other. By combining cloned embryos, you might end up with an embryo that's 99 percent reprogrammed rather than just 90 percent."

When McLaughlin and colleagues cut wild-type mouse embryos in half, they found that the expression of key developmental genes was not affected, suggesting that the developmental deficiencies of cloned embryos are not due to low cell counts alone. They speculate that cells in a blastocyst may communicate in a way that is compromised in a smaller cloned embryo.

McLaughlin's coauthors for the *EMBO Journal* paper include **Drs. Michele Boiani**, **Sigrid Eckardt**, **N. Adrian Leu**, and **Hans R. Schöler**—all of Penn's Center for Animal Transgenesis and Germ Cell Research. Their work was funded by the Marion Dilley and David George Jones Funds, the Commonwealth and General Assembly of Pennsylvania, the National Institutes of Health, the University of Pennsylvania Research Foundation, and the United States Department of Agriculture.

Pfizer Animal Health Gift

Pfizer Animal Health donated funds for the purchase of a plasma screen to be installed in one of the School's Multidisciplinary Laboratories. This will greatly enhance the teaching of histology and histopathology during rounds as images can be projected onto the screen from a microscope. These images are superior to those seen through a multihead scope and will provide students with more information.

Lushington

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which was a more tolerant state than Virginia, and stayed active in civic affairs most of his life. Dr. Lushington faced tremendous odds to become and practice as a veterinarian. His success can be measured in many ways. He was a veterinary doctor, and a parole officer, and a federal meat inspector. His community connections were strong: as a Mason, a deacon, and a member of the Chamber of Commerce. It was evident from spending time with Mrs. Moutrie that he was a wonderful, loving father who raised and educated two daughters, both of whom went on to prominence in the field of education.

Dr. Lushington and Dr. Lewis were at the forefront of the American veterinary profession, a field that is constantly changing. Until World War I, veterinarians were all men, and worked on large animals primarily. Today, the patients are predominantly pets, and women dominate veterinary classrooms. Over time, different animals and different animal diseases have changed how vets use their time and expertise. The Penn Veterinary School has survived these changes, which is an amazing economic feat. Penn's administration is a model of tolerance, and there are support centers for students in crisis. The School has learned that alumni veterinarians will stay connected to Penn throughout their lives if their school experience has been welcoming and positive.

The School has reached out to embrace its past in many ways. One example is through the gallery of photographs in the lobby of the Gladys Hall Rosenthal Building. Some photos depict century-old veterinary classes, professors, and buildings. Occupying a prominent space in the lobby gallery is a black-and-white photograph from the 1890s of a well-dressed, bespectacled young man—the picture of Dr. Lushington that I first saw on the Internet. With the placement of his photograph in the lobby, Dr. Lushington, one of our most distinguished alumni, now welcomes all who enter our School.

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