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First dog cloned

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Move over, Fluffy; cloning isn't just for cats anymore. The South Korean researchers who announced earlier this year that they had successfully derived stem cells from a cloned human embryo have now created the first-ever dog clone, a male Afghan hound, they report in *Nature* this week.

The puppy–named Snuppy for the researchers' Seoul National University–was born by cesarean section on April 24 to a yellow Labrador surrogate mother and turned 100 days old yesterday (August 2). A second cloned dog lived just 22 days before succumbing to aspiration pneumonia. A postmortem analysis showed no signs of "any congenital defect due to cloning," said Woo Suk Hwang, the leader of the Korean team. A third pregnancy resulted in a miscarriage.

Until now, somatic cell cloning in dogs has been hampered by limited success in maturing canine oocytes in vitro, said Hwang. Such maturation is necessary because unlike those of other domestic animals, canine oocytes aren't mature at ovulation. They're ovulated at prophase of the first meiotic division and undergo maturation in the distal part of the oviduct for at least 48 to 72 hours. The dog's opaque ova also make manipulation difficult.

Hwang attributed his team's success to their ability to produce a nuclear transfer construct using in vivo matured oocytes, to transfer it into a surrogate mother at an early stage of development without in vitro embryo culture, and to optimize the conditions for transfer "through trial and error."

"We were able to determine the exact ovulation and embryo transfer time," Hwang told *The Scientist* via E-mail. "Through hormonal and cellular analysis of vaginal smears, we made a database for prediction of ovulation time and for estrus synchronization. Thus, our team could obtain a good number of in vivo matured oocytes with good quality and find good surrogate mothers with an appropriate estrous cycle."

Altogether, the researchers collected an average of 12 oocytes from 123 donor females to create nearly 1,500 successfully reconstructed embryos. Of those, 1,095 were transferred back into the same 123 surrogates. The researchers used "naturally collected eggs" rather than the hormone stimulation typical of in vitro fertilization, coauthor Gerald Schatten, of the University of Pittsburgh, noted.

The team chose an Afghan hound because the dog was known to have a "gentle and docile pedigree," Hwang said. They also had access to a good collection of photos of the dog, which had unique fur color and appearance, when it was a puppy, he said, making it easier to distinguish whether the clone was identical. Microsatellite analysis of genomic DNA from the donor, the cloned dogs, and the surrogates confirmed that the clones were genetically identical to the donor.

Other animal cloning researchers hailed the report, but noted the low efficiency of transfer–2 live births out of 123 transfers, or 1.6%–and the greater availability of canine surrogates and ova in South Korea than in the United States.

"The efficiency is still pretty dismal," said Jorge Piedrahita, who studies animal cloning at North Carolina State University. Cattle embryonic transfer efficiency is about 10%, while pig efficiency is as

high as 8% to 9%. "The statistic they cite is somewhat misleading," Piedrahita told *The Scientist*. "It is not 1.6%; it should be 1 out of 1,095. It's an important advance, but I doubt the utility at that efficiency."

Phil Damiani, chief scientific officer of Genetic Savings & Clone, which announced in December 2004 that it made the world's first sale of a cloned cat, said the efficiency was "probably one of the lower ones ever done for cloned animals." The company had hoped to be the first to produce a cloned dog and a few years ago had a clone that nearly came to term, Damiani told *The Scientist*. The fetus was alive on ultrasound, but stopped breathing by the time it was delivered by cesarean section. The Korean team has "jumped ahead," he said.

Damiani said that his company remained convinced that their technology–which relies on chromatin transfer, rather than nuclear transfer, and egg and embryo assessment prior to cloning and transfer–would eventually make it possible to clone dogs commercially.

The company expects to be able to produce a cloned dog in the next few months, said Genetic Savings & Clone spokesperson Ben Carlson. "People have been asking us, does this mean that tomorrow you'll be able to start offering this service commercially? We wouldn't be able to make a successful business out of using the technique the South Koreans used," Carlson said. The low efficiency rate, combined with stricter animal welfare rules in the United States that limit the number of times eggs can be harvested and that transfers can be made, would make it impossible. But "it certainly validates our contention that dogs can be cloned," he said. "It doesn't mean we're quite there yet."

Schatten, who traveled to Seoul this past weekend, was quick to note that the team does not support the cloning of pets "or any other members of our family. Nuclear transfer should be restricted to medical research," he told *The Scientist* via E-mail. "This is not to make dogs by this unnatural method, but to advance stem cell science and medicine."

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