

Dolly Departs

Early 2003 has brought animal cloning into the headlines once again. Not the announcement of new clones; these headlines brought news from the other end of the spectrum, the passing of a famous clone and her counterpart.

Dolly, the image of cloning for many, has sparked debate at both ends of her life.

A cloning icon

On the 5th of July 1996, Dolly, the world's first clone of an adult mammal, was born. Dolly was cloned from an adult cell through nuclear transfer, research carried out jointly by scientists from the Roslin Institute and PPL Therapeutics. Cells were taken from the mammary gland of a pregnant sheep and cultured in the lab. The nucleus from one of these cells was transferred into an egg cell which had its original nucleus removed. The egg cell with new nucleus was stimulated to begin development then implanted in a surrogate mother. A healthy Dolly was born, genetically identical to the sheep from which the mammary cells were taken.

In fact, Dolly was healthy enough to produce multiple offspring. Dolly, a Finn Dorset, was mated with

'David', a Welsh Mountain ram. In 1998 the first lamb 'Bonnie' was delivered healthy and did well under the reported strong maternal instinct and enthusiastic mothering by Dolly. In 1999 Dolly's second pregnancy produced three healthy lambs after another mating with David. In all Dolly had six lambs.



Dolly, the world's first mammal cloned from an adult cell, with her first lamb.

Image courtesy of the Roslin Institute

News did come that Dolly may have had health issues, possibly related to being a clone. Genetic studies on Dolly suggested that the telomeres of her DNA were slightly shorter than would be expected in a sheep of her age. Telomeres are nubs of protein and nucleic acid that cap the ends of chromosomes. There is theory and some evidence that telomere length is linked to ageing. Shorter telomeres did not come as a surprise with Dolly and were in fact expected. Dolly's shortened telomeres may have been a result of her unusual origins: she was made using genetic material taken from a six-year old ewe, and therefore some of the telomere shortening could have been passed on; and the cloning procedure requires cells to be cultured in the laboratory for a period of time, further reducing the length of the telomeres.

It was also reported in early 2002 that Dolly had developed arthritis at the relatively young age of five and a half. The average lifespan of a sheep is 12 to 14 years. There is no evidence to show that the arthritis was a result of Dolly being a clone.

In February 2003, the world received news that Dolly was euthanased after developing a progressive lung disease at age six and a half. Lung infections and disease are common in older sheep, especially those housed indoors. A full post mortem was conducted and confirmed the cause of the problems as Sheep Pulmonary Adenomatosis (SPA), a virus induced tumour. The arthritis in her hind legs was also confirmed but no other physical abnormalities were found. Detailed examination will also be a part of the analysis. SPA is not uncommon in sheep in the 4-5 year range and there is no evidence that cloning was a factor in Dolly contracting the disease.

Dolly will be donated to the National Museum of Scotland where she will be prepared for display, continuing to be a part of cloning history.

Cloning down under

Researchers from the South Australian Research and Development Institute (SARDI) and the University of Adelaide produced a cloned sheep in 2000. Using technology based on that used to produce Dolly Australia's first cloned sheep 'Matilda' was produced, with hopes to help the nation's wool industry. The group believes that cloning techniques have the potential to shorten the time required by standard breeding strategies to develop premium wool types. Standard breeding can take up to 13 years to get the improved bloodline from the initial parent to the flock level. Cloning has potential to shorten this time to a single generation or one year. The technology could also have an impact in other areas, such as genetic rescue of flocks endangered by disease, or duplicating animals with special qualities nearing the end of their lives, again saving the genetic value.

Like Dolly, Matilda also produced offspring, though in a less direct manner. Using a technique known as JIVET (juvenile *in vitro* embryo transfer), eggs are collected from juvenile lambs, matured and fertilized. The resultant embryos are then transferred to host ewes. JIVET is not a cloning technique but more alike to *in vitro* fertilization, a technique often used for human parents. The researchers believe JIVET has potential to be a valuable breeding tool, with the possibilities of substantially reducing generation time thus increasing the rate of genetic improvement and allowing for the production of lambs with elite characteristics for breeders.

Unexpectedly Matilda died the same month as her counterpart Dolly. Observations of Matilda (throughout her life) indicated that she was a healthy animal, as are the offspring produced from her eggs. Matilda's cause of death was not known and an independent autopsy did not identify the cause of death. At the time of Matilda's death other clones produced by the same research institute were fit and healthy.

The early or unexpected death of these two clones has raised debate about the effectiveness of cloning technology. Some groups are even calling for a global moratorium on all experimental and commercial use of GM or cloned farm animals. In the science field others acknowledge that cloning is a very young technique, but with great potential and that continued research to improve and use the technology is very important.

For more information:

The Roslin Institute:

<http://www.roslin.ac.uk/>

AgBiotech InfoSource #28 - Cloning mammals:

http://www.agwest.sk.ca/event_inf_may97.shtml

South Australian Research and Development Institute:

<http://www.sardi.sa.gov.au/>

NewScientist.com - articles on cloning:

<http://www.newscientist.com/hottopics/cloning/>

How Stuff Works - cloning:

<http://www.howstuffworks.com/cloning.htm>

To find out more about agricultural biotechnology or to book a tour of the Saskatchewan Agricultural Biotechnology Information Centre (SABIC), contact:

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