IN THE NEWS

More than nine lives

"She may not look like much, but these are dramatic paws for science" says *The Guardian*, referring to Cc:, better known as Copy cat, the first ever cloned cat. Although the kitten was born on 22 December 2001, its existence was not made public until 15 February 2002. Cc:, who was cloned by nuclear transfer, "took the researchers 188 tries … [t]hey got 82 embryos but only one cat got pregnant, with a single kitten" (*CNN.com*). Despite being called Cc:, "she is not an exact copy of her mother, Rainbow" says *The Guardian*, and goes on to explain that her unique coat colour markings are "determined by events in the womb rather than by genes". The team of scientists at Genetic Savings and Clone, of College Station, Texas, and Sausalito, California, who are responsible for Cc:, say that they were "glad that the clone did not look like the original", because they have "been trying to tell people that cloning is reproduction, not resurrection" (*The New York Times*).

Cloning of Cc: "was financed by 81-year-old John Sperling who owns … Genetic Savings and Clone" (*Daily Mail*). The company is planning "to offer the technology to wealthy people seeking to replace their beloved pets" (*Daily Mail*) and is "already storing tissue from cats and dogs, for a fee" (*The New York Times*). Current predictions are that "cloned cats are likely to cost around £7,000" (*Daily Mail*), but dogs, which have yet to be cloned, would be more expensive. Although there are high hopes for the commercial success of pet cloning, many ethicists have spoken out against it, questioning "its usefulness and the welfare of the clones" (*The Independent*).

Magdalena Skipper

EVOLUTION

It can pay to be provocative

In 1988, John Cairns published a study claiming that *Escherichia coli* cells could respond to selection by directing advantageous mutations to specific genes. This process — adaptive mutation — presented a fundamental challenge to established views about the way evolution works. Not surprisingly, many geneticists responded by investigating whether this observation could be explained by more conventional mechanisms. Heather Hendrickson and colleagues now present just such a model for adaptive mutation, which might also be relevant to genetic changes that occur in cancer.

The experiment that started off the debate involved an *E. coli* strain that carried an F′ plasmid with a mutant *lacZ* gene. When the strain was incubated for several days on lactose-containing medium — lactose cannot be utilized by the Lac⁻ mutants — *lacZ* revertants slowly accumulated at many times the expected frequency. It looked like mutations were being directed to occur in the very gene required to get the cells growing again. Subsequently, the revertant colonies were shown to carry mutations elsewhere in the genome. This suggested that, in this system, selection induces a mutable state that increases the occurrence of useful mutations.

Hendrickson *et al.* propose a rather different model. The *lacZ* mutation is known to be 'leaky', so the authors suggest that, if the mutant gene is duplicated, there would be enough activity to support slow growth. Further amplification of the *lacZ* gene during growth of individual clones would confer an additional selective advantage. Recombination products derived from the repeated copies would then cause the induction of the SOS DNA repair system, leading to increased mutability and to occasional reversion of the *lacZ* mutation.

Finally, loss of mutant copies of the gene will turn off the SOS system, return the level of mutability to normal and leave cells with a stable Lac⁺ phenotype. So, adaptive mutation reflects a sequence of events, each of which confers a selective advantage.

The authors tested several predictions of the model, all of which were upheld: for example, when amplification was inhibited, reversion did not occur; the Lac⁺ phenotype of colonies with an amplified mutant *lacZ* gene was more unstable, relative to colonies that carry a reversion mutation; and mutations that abrogated the SOS response reduced, but did not abolish, the recovery of revertant mutations.

This model for adaptive mutation provides a neat explanation for the phenomenology of the Lac/F′ system, although this is certainly not the end of the story. However, the authors also discuss how this model could account for the accumulation of multiple mutations in tumour cells. A key point is that an initial duplication event provides sufficient selective advantage to initiate a clone within which secondary mutations can arise. So, although the concept of 'adaptive' mutation might gradually be eroded, the provocative claims associated with the initial observations have served to stimulate some exciting new ideas.

Mark Patterson

References and links

ORIGINAL RESEARCH PAPER Hendrickson, H. *et al*. Amplification-mutagenesis: evidence that "directed" adaptive mutation and general hypermutability result from growth with a selected gene amplification. *Proc. Natl Acad. Sci. USA* 2002 (DOI 10.1073/pnas.0326180899)
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