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Unmasking infertility in mice

For the first time, researchers have identified a mutation that causes autosomal-dominant male sterility in mice. Scientists hope further study of the mutant gene and its effects will lead to better understanding of infertility in humans.

Up to 15% of couples are unable to conceive due to defects in meiosis, the division of diploid germ cells to produce haploid gametes. Despite the prevalence of the problem and the despair it causes, little is known about the genetic underpinnings of infertility in humans.

Now, a research team led by John C. Schimenti of Cornell University (Ithaca, NY) reports that genetic screening of mice produced using chemically mutagenized embryonic stem cells led to the identification of a mutated version of the *Dmcl* gene, which is needed for meiotic recombination. A two base-pair change results in an amino acid substitution that arrests meiosis, preventing sperm production (*PLoS Biology*, May). Although female mice carrying a copy of the mutant gene are fertile, they exhibit high rates of abnormalities during meiosis. Nevertheless, because carrier females are able to reproduce, a dominant gene analogous to this one could propagate in human populations.

Rhesus macaque genome revealed

A consortium of researchers has assembled a high-quality draft of the genome of the rhesus macaque, the most widely used nonhuman primate in biomedical research.

The Rhesus Macaque Genome Sequencing and Analysis Consortium used whole-genome shotgun sequencing to assemble a draft sequence using DNA from a single macaque female and filled in the gaps using a bacterial artificial-chromosome library constructed from an unrelated male (*Science*, 13 April). The finished sequence had 93% homology with the human genome.

The list of research breakthroughs involving the rhesus macaque (*Macaca mulatta*) is a long one, including such watersheds as the discovery of the Rh blood groups and the cloning of the first primate. The sequencing of the macaque genome should make it an even more valuable research animal by helping researchers to better understand the genetic basis of physiological, anatomical, and behavioral differences between humans and monkeys. In addition, the rhesus genome should also allow researchers to garner more information from the human and chimpanzee sequences by providing a point of comparison for the genomic data. Sequencing of several other nonhuman primate species—including the orangutan, gibbon, and marmoset—is currently underway; once these sequences are available, researchers will have even more information to use in finding what genes differentiate humans from our primate relatives.

A new path to stop cancer

By investigating more closely the consequences of short telomeres for chromosomes, scientists have found a novel pathway for suppressing tumor growth in a mouse model of blood cancer.

Since the 1990s, when the shortening of telomeres—repetitive bits of DNA at the end of the chromosomes—was first described in human cells, the scientific community has been interested in targeting telomeres for cancer therapy because they are critical for cell survival. Indeed, by inhibiting telomerase, the enzyme that maintains the chromosome ends, some mouse studies have shown that cancer growth can be suppressed. In those studies, the cancer was stopped by apoptosis, a process of cellular suicide.

Now, a group led by Carol Greider at the John Hopkins School of Medicine (Baltimore, MD) has added to those findings by demonstrating that short telomeres can also stop cancer progression via another pathway. Greider and her colleagues crossed mice that were unable to produce telomerase with mice that model a rare aggressive human cancer, Burkitt's lymphoma. As expected, apoptosis prevented the tumors of these mice from developing. To their surprise, however, the short telomeres still prevented tumor development even after blocking apoptosis. Instead, the tumors entered senescence, in which cells cease to divide (*Cancer Cell*, doi:10.1016/j.ccr.2007.02.026). That telomerase inhibition induces two parallel mechanisms for suppressing tumor growth may help researchers develop more comprehensive cancer treatments.