



DNA Circles Cause Cow Coat Color Changes

Keith Durkin wasn't trying to figure out why some Belgian Blues, a cattle breed known for its big muscles, have a wide white stripe down their backs. And the young geneticist certainly didn't expect to uncover what seems to be a new way that a cell shuffles its genes around. A postdoc at the University of Liège in Belgium in 2009, Durkin was scanning a database containing the genotypes of 4400 animals to flag duplicated chromosomal regions. One such region, which showed up in nine of the cattle, caught his eye because it included a gene called *KIT* that is involved in coloring animal coats. When he checked on those nine, each animal had the telltale white stripe.

Durkin was a little puzzled at first because the database information suggested the repeated DNA was on chromosome 6. His University of Liège colleague Carole Charlier had been homing in on the mutation for this "color-sided" trait and had seemingly localized it to chromosome 29, not chromosome 6. By using fluorescing tags that home in on specific pieces of DNA, Durkin and his colleagues showed that a copy of a piece of chromosome 6 had at some point jumped to chromosome 29. It seems that when the 480,000-base-long stretch of DNA broke away, *KIT* became separated from some regulatory DNA, and the subsequent misregulation led to the unusual coat color pattern.

But the sequence of the duplicated region on chromosome 29 was also somewhat confusing. The researchers could tell from the chromosome 6 sequence what the beginning and end of the duplicated DNA should be, but these sequences were instead in the middle

of the chromosome 29 copy. When the segment jumped out of chromosome 6, Durkin concluded, it must have formed a loop of DNA that then broke apart in a different place before inserting into chromosome 29. Imagine forming a circle out of a sequence of letters, such as A, B, C, D, E, and F, then snipping that loop someplace different from where the ends originally joined. If the break came between C and D, for example, the new linear sequence would be D, E, F, A, B, C.

Durkin's story doesn't end there. In color-sided Brown Swiss cattle, he and his colleagues found that the *KIT*-containing chromosome 29 segment had copied itself into another loop and then hopped back into chromosome 6 next to the original sequence. Durkin also found scrambled duplications of this DNA sequence in other color-sided breeds, including distantly related cattle from Ireland and Ethiopia. That observation suggests that this circularized DNA shuffling must have occurred early in the development of cattle breeds.

Geneticists say they haven't seen genes move between chromosomes in quite this way before. "The circular mechanism is really novel," says Douglas Antczak, a veterinary geneticist at Cornell University. "The mechanism by which fragments of genes go to another place is not well-known," adds Xavier Estivill, a geneticist at the Center for Genomics Regulation in Barcelona, Spain. There is a group of so-called transposable elements called Heliotrons that also seem to jump around the genome as circles of DNA, but the sequences of the circles in these cat-

Circles for stripes. Belgian blue cattle got white back stripes from DNA circles moving a gene.

tle look nothing like these transposable elements, Durkin says. Estivill wonders whether this circle-driven, gene-shuffling mechanism will prove common. "We are now trying to find some examples in humans," he says. —E.P.

On the Trail of Brain Domestication Genes

Domesticated animals have far more in common than service to humankind. As Charles Darwin observed, compared with their wild counterparts, dogs, pigs, and cattle tend to be smaller, have finer bones, and sport spotted coats. Domesticated animals generally are also less aggressive, less fearful, and more playful.

Fascinated by these behavioral similarities, Svante Pääbo, Frank Albert, and their colleagues at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, wondered whether these tamed species—and perhaps even some primates, including humans—also share similar patterns of gene expression in their brains. Researchers as far back as Darwin have speculated that humans underwent "self-domestication," and, more recently, Brian Hare of Duke University in Durham, North Carolina, proposed that bonobos evolved domesticated behavior to encourage group living.

To explore this issue, Albert, now at Princeton University, turned to the genes active in the prefrontal cortex, which is responsible for long-term planning and associative thinking. Albert isolated genetic material representing active genes from the prefrontal cortex of a half-dozen dogs and wolves, as well as from the brains of a half-dozen domestic pigs and rabbits and their wild counterparts. He sequenced these genetic fragments to determine the genes from which they derived and then estimated each gene's level of activity by quantifying how often his sequencing highlighted it.

He looked for genes whose activity was increased or decreased in the three domesticated species compared with in the wild ones. He found 60 such genes and then sought confirmation by doing a similar comparison of the domestic guinea pig and its close wild relative, a cavy. About 40 of the 60 genes displayed the same boost or drop,