Researchers take first look at the genetic dynamics of inbreeding depression

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Declines in reproductive success due to inbreeding are probably due to a few key genes that influence other genes, said Illinois animal biology professor and department head Ken Paige, who led the study. Photo by L. Brian Stauffer, U. of I. News Bureau

Researchers have taken a first look at the broad genetic changes that accompany reproductive declines in inbred populations. Although scientists have known for more than a century that small populations of closely related plants or animals are likely to suffer from low reproductive success, the exact mechanism by which this "inbreeding depression" occurs is still the subject of debate.

The new study, in Conservation Biology, is the first to look at inbreeding depression as it relates to the expression of all of an organism's genes - to see which are more or less active in inbred populations and what they do.

By mating male and female fruit flies that were genetically identical to one another, researchers at the University of Illinois were able to determine how much the flies' genetic likeness reduced their reproductive success. They repeated the experiment in six lines of fruit flies that were identical to one another except for the composition of one of their chromosomes; only the genes of chromosome three differed between the lines.

The researchers also crossed the three highest inbred lines to one another, creating outbred lines that could be compared with the inbred ones.

Using oligonucleotide microarrays, which can measure the activity of all of an organism's genes at once, the researchers were able to see which genes were more or less active (up-regulated or down-regulated) in the inbred versus the outbred lines.

The six inbred lines of fruit flies showed a lot of variation in the degree of inbreeding depression, from 24 to 79 percent when compared with non-inbred flies. The researchers also found that 567 genes in the high inbreeding depression lines were expressed at higher or lower levels than the same genes in the other inbred lines. Only 62 percent of these genes were located on chromosome three (the only chromosome that differed between the lines) indicating that variation in chromosome three had altered gene expression on the other chromosomes.

"These results suggest that a significant amount of inbreeding depression is due to a few key genes that affect the expression of other genes," said animal biology professor and department head Ken Paige, who led the study.

Of particular note were identical changes in the expression of 46 genes in all three of the high inbreeding depression lines, Paige said, making them of interest for further study.

Genes associated with inbreeding depression could be grouped into three broad categories of function: those involved in metabolism, stress, and defense. This is a surprising finding, Paige said, "because we think of inbreeding as a random process."

Many metabolic genes were up-regulated in the inbred flies, as were genes that fight pathogens such as bacteria or viruses. A third group of genes was down-regulated. They code for proteins that protect the body from reactive atoms and molecules that can damage cells.

These changes in gene expression are shunting energy away from reproduction and undermining some basic cellular functions, Paige said.

Inbreeding depression is thought to result from a deleterious pattern of inherited genes. In general, an organism with two parents has two versions of every gene - one maternal and one paternal. These different flavors of a gene are called alleles. If the maternal and paternal alleles differ, one of them usually dominates, conferring all of its qualities to the offspring. The other, silenced allele is called "recessive."

Some alleles are detrimental to health. Most of these are recessive, meaning that they do not cause problems unless the organism inherits two copies of them - one from each parent. When the alleles differ, one (the dominant allele) often masks the deleterious effects of the other.

But the interaction of parental alleles in their offspring can be quite complex. Sometimes an allele causes a disease or disorder even if it is paired with a different allele. Sometimes several genes influence a single trait. And sometimes two different alleles can lead to a higher level of gene activity than occurs in either parent (this last phenomenon is called overdominance).

When closely related individuals mate, their offspring are likely to end up with identical alleles for many traits. Many potentially harmful recessive alleles are no longer masked by dominant alleles, so more genetic disorders arise. Similarly, offspring that inherit two identical alleles for some traits will also lose any advantages once conferred by overdominance.

Biologists have long wondered which of these mechanisms causes the reproductive failures seen in inbred populations. "It's still being debated," Paige said.

The new study found that about 75 percent of the reproductive declines seen in the inbred flies could be attributed to the loss of dominant alleles and the subsequent "unmasking" of deleterious alleles. More surprisingly, the data also indicated that 25 percent of the declines were due to the loss of overdominance.

"That means we have two mechanisms ongoing," Paige said. "One does predominate, but the other may be important, too."

The fact that a relatively large number of genes are affected by inbreeding is bad news for conservationists hoping to save small populations of plants or animals from extinction, Paige said.

It means that there is no easy fix to the problem of inbred populations. The best approach is to try to preserve and maintain genetic diversity in natural populations well before they begin their slide into an "extinction vortex," he said.

Source: University of Illinois at Urbana-Champaign (news : web)

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