Anonymous. Gene-blues for the cheetah. New Scientist [16 May 1985], 21. 1985.

Keywords: Acinonyx jubatus/cheetah/genetic variation/genetics/Major Histocompatibility Complex

Abstract: Lack of genetic variation threatens the survival of the cheetah. Research produced evidence of poor reproductive success and vulnerability to diseases.

Gene-blues for the cheetah

THE CHEETAH is its own worst enemy, according to recent genetic studies. Biochemical analysis of enzymes and other proteins shows that the species has 10–100 times less genetic variation, or polymorphism, than is normally found in mammals. This causes a number of problems, all of which are important if the cheetah is not to become extinct.

Cheetahs have poor reproductive success, both in the wild and in captivity. Their semen contains only one-tenth the number of sperms found in the semen of domestic cats, and up to 71 per cent of their sperms are abnormal. Infant mortality in the wild is estimated to be as high as 70 per cent, and data from breeding programmes worldwide show that, on average, 29 per cent of cheetahs born in captivity die before the age of six months.

The genetic constitution of the species resembles that of highly inbred livestock, probably due to a severe reduction in numbers—a population bottleneck—in its evolutionary past. The implications for conservation are particularly serious, because the cheetah is already one of the most endangered of all the cats.

Now, research by a joint team of scientists in the US and South Africa, led by Stephen O'Brien of the National Cancer Institute in Maryland, has produced further evidence of the Cheetah's genetic malaise and its vulnerability to disease (*Science*, vol 227, p 1428).

The time taken for skin grafts between unrelated cheetahs (allografts) to be rejected provided researchers with an estimate of genetic variability in the cheetah's immune system. All mammals produce antigens responsible for allograft rejection. These antigens are genetically determined by one particular chromosomal segment known as the major histo-compatibility complex (MHC). The MHC normally shows more polymorphism than any other genetic locus of vertibrates, and so allografts between domestic cats are rejected suddenly and rapidly, 7–13 days after grafting.

Jeremy Cherfas

Lack of genetic variation threatens the survival of the cheetah

Allografts between 12 South African cheetahs showed no rapid rejection. Three individuals rejected slowly, at 39–70 days, but all other grafts were apparently accepted. So there was a high degree of shared MHC antigens in the group tested.

The main function of the MHC, however, is in immune defence against infection organisms. Lack of genetic variability in the MHC may explain why an outbreak of feline infectious peritonitis (FIP) killed 18 of 42 cheetahs at a wildlife park in Oregon in 1983. FIP is caused by a virus and is seldom fatal in domestic cats. Could this have been a particularly virulent form? This is unlikely, because attempts to transmit the disease by injecting it into domestic cats failed. African Lions exposed to the disease also failed to develop symptoms.

Some genes at the MHC are known to vary in how much they control the ability to develop antibodies to viruses, and others play a major role in the ability of defensive T-cells to recognise and destroy cells infected with viruses.

The researchers suggest that lack of polymorphism in the MHC might limit the variety of viral antigens that T-cells are able to recognise. This can leave a population such as the Oregon colony wide open to attack by a virus that has adapted to take advantage of a gap in the repertoire.

The outlook is not entirely bleak, however. The development of effective breeding programmes has helped other inbred species, such as Père David's Deer, survive. In the wild, the northern elephant seal suffered a population bottleneck in the last century due to overhunting. It too has critically low genetic variation, but has nevertheless made a successful comeback on the Californian coast.

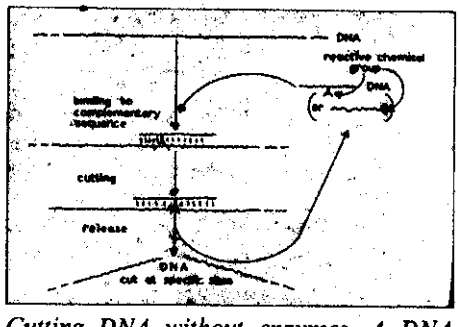
Also, cheetahs in East Africa which have not yet been investigated may provide some much needed genetic variety. □

Genetic engineering without enzymes

THE TOOL KIT of the genetic engineer consists largely of a selection of enzymes that can be used to cut, alter, stitch and copy genetic material on demand. These enzymes are very specific in cutting, for example, only at particular sites of defined nucleotide sequence. A more generally useful set of tools would retain the specificity of enzymes, but would place it under our control; allowing scientists to manipulate *any* desired nucleotide sequence rather than being limited by the natural preferences of enzymes.

As a first step towards such a versatile specific toolkit, two separate teams of American scientists have found a way to cut single-stranded DNA anywhere they choose.

The general strategy is very simple (see Figure). First, a short stretch of DNA is made which can bind by base-pairing to the DNA sequence you wish to cut open. This "complementary DNA probe" is then linked to some reactive chemical group which, like a pair of molecular "scissors", is able to cut the backbone of DNA. The activated probe can then be added to the target DNA under conditions that allow it to bind to the target sequence and cut it open.



Cutting DNA without enzymes. A DNA probe is made and attached to a chemical group that can snip DNA. These "molecular scissors" are made specific by altering the sequence of nucleotides in the DNA probe

Using the same overall strategy (but different probes) Barbara Chu and Leslie Orgel of the Salk Institute, and Geoffrey Dreyer and Peter Dervan at Caltech, consistently cut target DNAs at or very close to particular chosen sites (*Proceedings of the US National Academy of Sciences*, vol 82, p 963 and p 968).

These reactions did not quite have the exquisite specificity of enzymes. Chu and Orgel found that the cutting took place anywhere within a stretch of DNA about 9 nucleotides long; while Dreyer and Dervans' scissors cut a swathe spread across a 16 nucleotide long region. But both groups are hopeful that this reasonable specificity will be further improved as the technique develops.

The technique seems equally suited to cutting RNA, and could develop into a very useful addition to the genetic engineer's tool kit. It may make it easier to investigate and exploit the genetic information of large genomes (the total collection of genes on a chromosome) by chopping them up into specific short sections. It may assist studies of gene control and gene activity by allowing particular messenger RNAs to be cut up and therefore destroyed. It may even find eventual use in chemotherapy as a means of destroying the DNA or RNA of pathogens such as viruses.

The possibilities will broaden considerably if the same basic strategy can be applied to things other than simply cutting target nucleic acids. By linking different reactive chemical groups to the DNA probes it may become possible to mutate and modify chosen sites on DNA or RNA in a whole series of different and highly specific ways. Provided they can be made sufficiently specific, these simple and versatile "enzyme-analogues" might have a big future. □