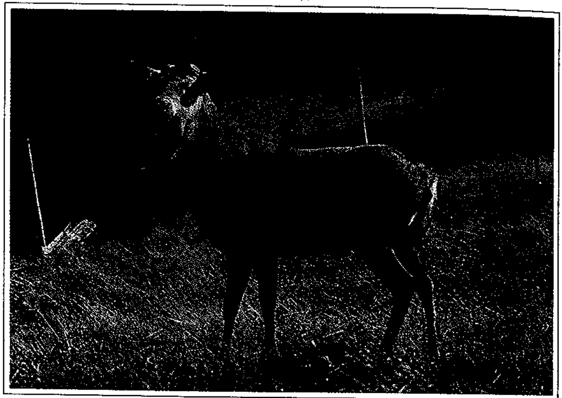
Map of the genes



Health in them thar genes

With the new science of gene mapping, it may be possible to breed disease-resistant deer without having to expose them to the disease itself. As **Craig Matthews** explains, researchers will be able to short-circuit the time consuming, ethically sensitive and costly methods used today.

SINCE 1953, when scientists Watson and Crick figured out that DNA (deoxyribonucleic acid) was in fact the molecular message of heredity, scientists have been working on ways to apply this knowledge to practical effect.

One application is to locate genes that cause resistance to disease. New Zealand deer scientists Mike Tate and Allan Crawford from the University of Otago, and Colin Mackintosh from AgResearch Invermay are doing important work in this area.

New Zealand farmed deer are very useful for this kind of study because the farmed deer population includes a variety of different deer species, subspecies and strains of deer.

All have distinct differences in their susceptibility to disease. Malignant catarrhal fever is a dramatic example. Pere David's deer and Sika are highly susceptible, whereas Wapiti are relatively resistant and Red deer show intermediate resistance.

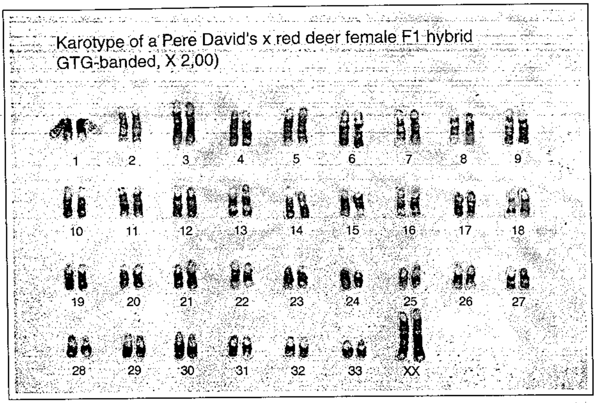
Because these differences are found in animals farmed in a common environment, it clearly indicates that these differences are the result of the animals' genes. Gene mapping is the tool that allows the location of these genes to be determined.

Right around the world, scientists are drawing the maps of genes covering the whole animal kingdom from fruit flies to humans

Gene mappers are interested in how the DNA fits together. They chop chromosomes into bits, breaking them up at convenient spots, and then try to put the bits back together in the right order. It's like doing a jigsaw puzzle or solving a code.

Sometimes, there are "signposts", called genetic markers, that make it easy to locate a particular region where a gene may be found (see panel).

It sounds simple when written over the space of a couple of sentences. In fact, it's a piece of scientific detective work that even Sherlock Holmes would have been proud of.



34 chromosomes of a female Pere David/Red cross, magnified 2000 times
Between them, these genetic "nations" contain all the information required to make a deer

For example, imagine for a moment that a single cell is represented by planet earth, and that you are observing "earth" from the moon through a telescope. Observing the chromosome would then be like magnifying the view so that an individual nation, say New Zealand, could be seen.

Genetic markers show researchers the general location where a gene is likely to be found. This would be like further magnifying the view so that Auckland could be picked out.

To locate a gene would then be like trying to find one street in the city. Then, if you wanted to know how each gene fitted together (the DNA sequence) it would be like knowing the addresses of individual houses on the street.

The AgResearch team is constructing a gene map of deer in order to determine exactly what chromosome segments are responsible for disease resistance and other traits.

The use of Pere David and Red hybrids has allowed very rapid progress in the initial stages of map construction, by allowing landmark genetic markers from each deer chromosome to be ordered.

These hybrids are important because gene markers originating from Pere David parents can be easily distinguished from those of Red deer. By seeing which Pere David gene markers can be passed on from generation to generation it is possible to work out the relative order of these gene markers on the gene chromosomes.

Once this framework of markers or "map" covering each of the deer chromosomes has been established, it can be rapidly adapted for use in a variety of herds and deer species to find chromosomes which carry genes for disease resistance.

An unexpected bonus of the gene mapping work in deer and other mammals is that the deer map appears to be very similar to the cattle and sheep gene maps, and has many similarities with the maps of humans and mice.

These similarities provide a second dovetailing approach to searching for genes in deer. For example, knowing where the gene for a particular trait is in the mouse and human chromosome gives important clues to its location on the deer chromosome.

The deer mapping team wants to use mapping and marker technology to identify genes with resistance or susceptibility to major deer diseases. The genes behind tuberculosis, internal parasitism and malignant catarrhal fever are ideal for this kind of technology.

In future their work may lead to simple DNA tests needing only a drop of blood, or a single hair follicle from an animal, helping breeders select disease resistant deer and identify highly susceptible animals before they are exposed to disease. □

Mapping the markers

MAPPING IS a way of locating and identifying genes which carry the chemical instructions that determine an organism's traits.

Some genes provide living things with protection against disease. By isolating a particular gene, scientists can map its place on the chromosome.

The importance of the gene map is that it provides a way to search for genes that confer disease resistance.

In trying to locate various genes, so-called genetic markers are vital. Imagine them as signposts that provide evidence that the gene one is trying to find is close by.

It's like knowing that Albert St, for example, is near Albert Park in Auckland. As Albert Park is such as obvious feature on the Auckland cityscape it acts as a marker for finding surrounding streets.

The key feature of gene markers is that they show variation or polymorphism — physical differences between individuals.

The trick in this kind of work is to find a polymorphism that coincides with the occurrence of a disease.

If a genetic defect that causes a disease is situated close by the gene that controls an innocuous polymorphism, it is said to be linked to that polymorphism. Close enough, and they tend to travel together generation after generation, despite all the shuffling of genes that normally takes place during reproduction.

So, if a certain pattern of polymorphisms coincides with the occurrence of the disease itself, and you know the location of the gene behind the normal polymorphism, it can be a strong clue to the location of the disease itself.

This association of polymorphisms is a genetic marker. To geneticists wandering around the chromosome unaided by a good map, genetic markers are molecular landmarks, like Albert Park is a marker for finding your way around our hypothetical Auckland. *— Craig Matthews*