

BIOTECHNOLOGY IN ANIMALS

It is hard to ignore the fact that biotechnology is becoming part of our everyday lives. For the past decade we have debated the pros and cons of these technologies being used in plants and food production.

Today, the technology is also being applied to animals, and in some cases, humans. What are the issues? What is fact, and what is fiction? To debate the issues, you need information.



What is biotechnology?

Biotechnology is a combination of two words – biology and technology.

Biotechnology then is the study of living things (biology) to create useful products. This includes agriculture, production of foods and medicine, cleaning the environment, and creating renewable energy sources. Many people confuse the term biotechnology with genetic manipulation or cloning. These areas form only a small part of biotechnology. Selective breeding and crossbreeding of species, fermentation, development of antibiotics and vaccines, and using biological controls to reduce feral animal populations are other examples of biotechnology.

It's in the genes

Gene technology is a new area of biotechnology, made possible by a greater understanding of the role of genes and the function of DNA.

Being able to change the behaviour or characteristics of genes has only been possible in the last few decades. Genes are segments of DNA that provide a code to produce a particular protein within a cell. These proteins then do all the work of constructing, maintaining and building the organism they are part of. The entire length of DNA inside a cell is made of genes and extra 'spacer' DNA, the function of which is yet unknown. Humans have about 25,000 genes in their DNA. Each one of these genes contains instructions to make proteins that keep our body ticking.

When you look at the genes of various organisms, it is amazing how similar some of us are. Apes and humans share 98 per cent of their genes; humans and mice share at least 80 per cent; and a human and a cabbage share between 20 and 40 per cent. Fortunately, adding mice genes to a cabbage will not produce a human.

Reading the gene story

Knowing which genes are in an organism and the role that they play is extremely useful. Medical scientists are investigating diseases such as muscular dystrophy and diabetes to determine which genes cause them and how gene engineering could provide a treatment. 'Reading' genes can also be used to detect viruses. Viruses contain genes, and when they invade a host cell, they use that cell to produce their own viral proteins. Scientists can look for evidence of these proteins to determine if a cell is infected with a virus.

Tweaking the genetic dials

Throughout history, humans have influenced the characteristics of plants and animals through selective breeding. For example, the vast range of dog breeds that exist today are the result of selective breeding. Wheat is another example of selective breeding. In 1901, William Farrer began marketing a new strain of wheat called Federation, which

he developed after years of crossbreeding various strains of wheat.

Precise breeding

Today, science has given us the ability to identify the genes within an organism that affect one, or some, of its characteristics. By understanding what a gene does within an organism, we can manipulate how and

when the gene is active. This is known as genetic manipulation. Alternatively, once a gene's function is known, animal breeders can select animals that naturally have any beneficial genes for future breeding programs. Over generations, a greater proportion of animals in the herd or flock will carry the beneficial genes.

Less is more

A new blood test is helping pig and cattle breeders select animals that are the most efficient at converting their food into muscle rather than producing fat.

The Adelaide-based company, Primegro Ltd developed the test, based on the amount of a protein called Insulin-like Growth Factor-1 (IGF-1) that circulates in an animal's blood. Animals that produce lower levels of IGF-1 will have a better feed conversion rate – or better efficiency. A more efficient animal is one that needs less food or energy to grow, or one that is leaner and produces proportionally larger amounts of muscle.

IGF-1 levels are heritable, meaning that these performance characteristics are passed on from mum and dad to the next generation. The technology is already being used, in combination with other genetic evaluation procedures, by Australian and international farmers to improve their breeding programs through the more accurate selection of superior offspring.

Biotechnology is helping farmers to breed leaner pigs.



CSIRO Livestock Industries

Amplifying prawn viruses

Prawns and other crustaceans are a popular food source for people worldwide. Unfortunately, some oceans are being over-fished and many fish populations are in danger of collapse.



To combat this, many countries, including Australia, are developing prawn farms. But with any farm-raised animal there is potential for the outbreak of disease. CSIRO Livestock Industries has developed a virus-

detection kit that uses a polymerase chain reaction (PCR) to identify the presence of disease-causing viruses in prawns.

A PCR acts like a photocopier, creating multiple copies of a gene sequence to

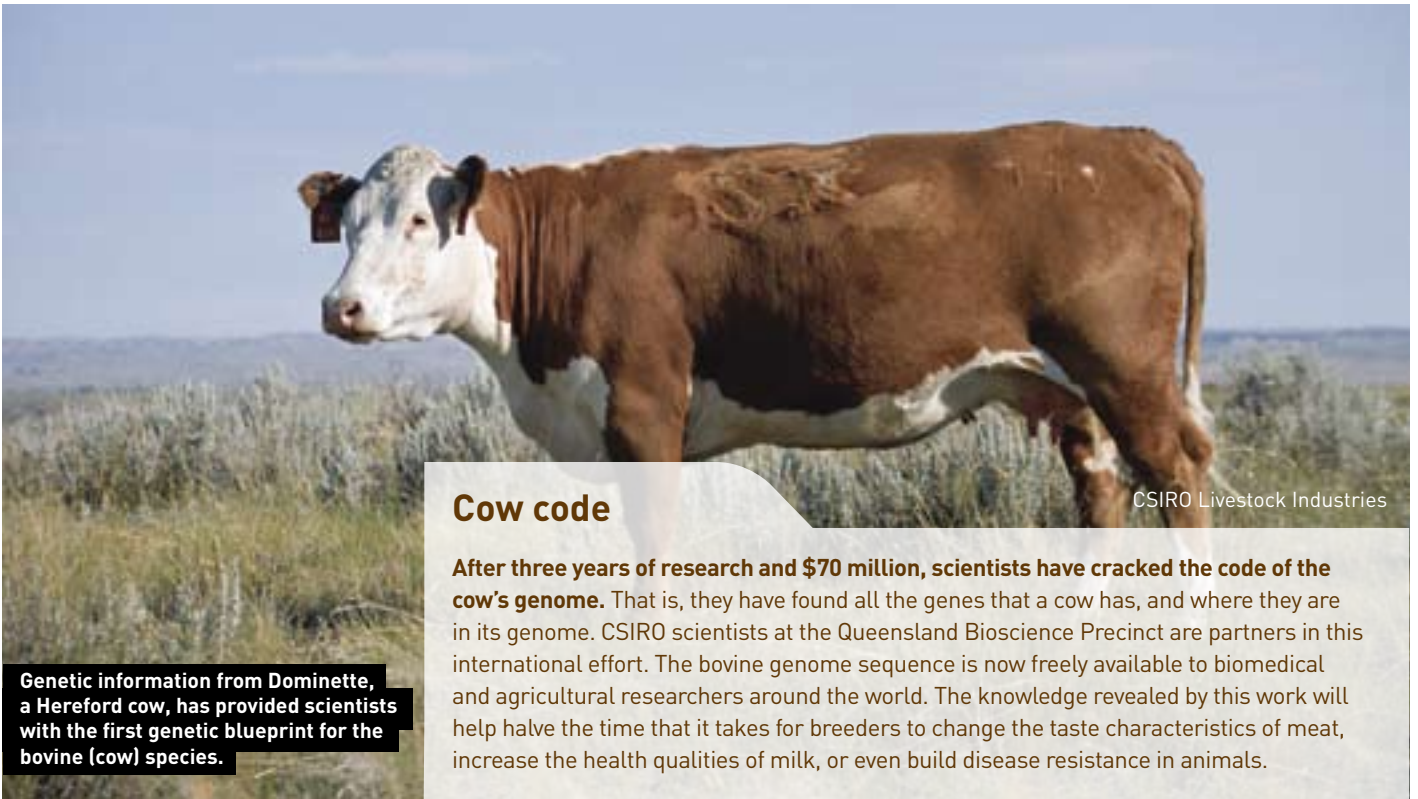
make it easier to identify. The CSIRO kit is so good at performing this task that it can detect a virus before it appears as an infection in the prawn or spreads to other prawns.

CSIRO Marine Research

Gene hunters

A \$30 million Sheep Genomics Program, supported by a variety of research institutions, together with Meat and Livestock Australia and Australian Wool Innovation, has set researchers forth on a hunt for sheep genes associated with wool and meat quality, parasite/disease resistance, and reproduction.

Screening tests are some years away, but if and when they are developed, breeders will be able to improve stock quality, simply by breeding with animals that possess desirable genes or do not have unwanted genes.



CSIRO Livestock Industries

Cow code

After three years of research and \$70 million, scientists have cracked the code of the cow's genome. That is, they have found all the genes that a cow has, and where they are in its genome. CSIRO scientists at the Queensland Bioscience Precinct are partners in this international effort. The bovine genome sequence is now freely available to biomedical and agricultural researchers around the world. The knowledge revealed by this work will help halve the time that it takes for breeders to change the taste characteristics of meat, increase the health qualities of milk, or even build disease resistance in animals.

Genetic information from Dominette, a Hereford cow, has provided scientists with the first genetic blueprint for the bovine (cow) species.

Omega lamb

Lamb could soon be a source of the same healthy fats found in fish oil, which nutritionists are saying we should eat heaps of.

Researchers at CSIRO Livestock Industries, working in collaboration with the Western Australia Department of Agriculture, have found naturally high levels of omega-3 fatty acids in some sheep, and also established that this is a heritable trait. This means that it is possible to breed sheep to have high levels of these healthy fats.

Step One is to find the sheep whose meat is naturally stuffed with these fats to use in the research team's breeding program. Once it has established a breeding line with consistently high levels of omega-3s, the team will hunt for the genetic markers which indicate that a sheep has the right omega-3-

making genes. Sheep breeders will then be able to test their sheep for these markers, and breed from those with the right omega-3 markers to produce a flock of sheep with healthier meat.

And pigs... too

This Australian research does not involve genetic modification of animals, but scientists in the US have succeeded in cloning pigs that produce omega-3 fatty acids in their tissues and organs. They took a modified version of a gene commonly found in the roundworm *C. elegans* and inserted into foetal pig cells. The scientists were able to create cloned pig embryos that grew into animals with higher than normal levels of omega-3s.



CSIRO Textile and Fibre Technology



Given that genetic transfer is possible, should this be explored further? Could the lessons we learn from perfecting these techniques help save humans and other animals?

Slicing and splicing DNA

Gene transfer, also known as transgenics, occurs in nature as well as in laboratories. In nature, viruses and bacteria are always swapping genes or inserting them into the genomes of other organisms. In the lab, scientists make a copy of a gene or genes responsible for certain characteristics in one organism, and insert them into the genome of another organism. This happens at the early embryo stage. The genes that have been added to the organism might provide an additional characteristic or enhance one that it already has. If an organism has a gene from another organism inserted into its DNA, it is known as a transgenic organism.

Medical milk

One application of the technology that has been tried in dairy cattle and goats was to add new genes that altered the composition of their milk so that it includes a beneficial protein to improve consumer nutrition or even treat a disease. All these experiments, however, are still in the early stages of research.

Medicine cow

Hematech, a biotech company in the United States, is trying to make a cow that can be used as a production system for human polyclonal antibodies. Polyclonal antibodies can be used to treat infections, cancer, organ transplant rejection and auto-immune disease. The only source of polyclonal antibodies at the moment is people who volunteer to donate blood plasma.

To make their cow, the company has genetically modified cow cells to carry human antibody genes. The cow antibody genes are inactivated, and these modified cells are then cloned to make embryos, and ultimately cows.

Polyclonal antibodies are produced in the body in response to a disease-causing agent, for example a virus. The genetically modified cows are given an immunising vaccine, which is effectively a weakened virus. In response, the cows make human polyclonal antibodies. Blood is taken from the cows, the polyclonal antibodies extracted and then purified, ready for use in treating human disease. This research, however, is still in the early stages. More research is needed to perfect the techniques and to make sure the polyclonal antibodies are safe and effective when used in humans.



Clones are animals two!

In biotechnology, cloning possibly generates the greatest number of questions. Is it ethical? What are the benefits? Could we be creating a generation of animals susceptible to one disease? Although scientists are aware of these issues, nobody yet knows all the answers.

At the moment there are two methods of cloning. The first method is known as embryo splitting. Before an embryo has reached 32 cells in size, it is split into two distinct embryos. Genetically, these two embryos are virtually identical, and this process could be repeated to produce more clones. Identical twins are clones.

The second method of cloning is nuclear transfer. In 1997, Scottish scientists created a lamb from the cell of an adult sheep. The nucleus of an unfertilised egg was removed and the egg (without its nucleus) was then fused with the nucleus taken from the cell of an adult sheep. An electric pulse caused the cell to begin

dividing and form an embryo, which was then placed into a ewe. Several months later, Dolly the sheep was born.

Nuclear transfer cloning is a difficult process. Of the 227 adult cells that were fused with eggs, only 13 pregnancies resulted, and Dolly was the only lamb born alive. In 2003, Dolly was 'euthanased' at the age of six years, after tests revealed she had a progressive lung disease. Today, the cloning 'strike-rate' is improving, with between one and 10 per cent of cloned cells surviving and becoming multi-celled organisms. And the clones now survive better and live longer. It's not perfect, but the technology is improving.

Why clone animals?

While the science surrounding nuclear transfer cloning is still in the developmental stage, embryo splitting is well understood and used in many areas of livestock industries and animal conservation. Cloning animals that exhibit a new or enhanced characteristic is more exact than using conventional breeding.

The DNA that each animal possesses is identical to the DNA from the donor, and unlikely to have been affected by environmental factors during the early stages of growth, which is the case with selective breeding. Therefore, the same desirable trait or product of an animal is present in each offspring. This is why genetically enhanced or modified plants and animals are cloned.

Matilda, Australia's first cloned sheep

In 2000, Dr Simon Walker and his team at the South Australian Research and Development Institute (SARDI) successfully produced Australia's first cloned sheep, Matilda.

Matilda was produced using techniques similar to those that produced Dolly. In February 2003, Matilda died of natural causes at three years of age. Since Matilda's birth, four more cloned sheep have been born and continue to show excellent health.

In collaboration with the University of Adelaide, the SARDI team is now looking at how cloned animals perform under various conditions. A cloned sheep provides a good mammalian model to

understand which genes are switched on or off at each stage of development. But because cloned sheep have a higher mortality rate at or soon after birth, the scientists are going back to the laboratory and investigating developmental influences at a cellular level. This will hopefully lead to more efficient cloning and an understanding of the factors that influence the wellbeing of both the foetus and the newborn offspring.

Cloning around

Worldwide, animals that have been cloned include mice, goats, cattle, pigs, rabbits, monkeys, cats, a horse, a mule, a banteng, a gaur (wild cow), and, most recently, a dog. In December 2004, a private company in the United States announced the first known sale of a cloned pet (a cat).

Photo above: One of SARDI's four recent clones, Annabel with her own lamb.

How to milk a wallaby

The hunt is on for genes in dairy cows that can improve the value of their milk. These are the genes that control milk production and the production of milk's bioactive compounds that have health-giving properties. But scientists are not searching in cows.

They are searching for the same or similar genes in some of Australia's iconic animals, such as the tiny tammar wallaby, fur seal, echidna and platypus.

Weird? Not really. For example, after a short pregnancy, the tammar wallaby gives birth to a tiny embryo-like joey. Instead of a placenta delivering nutrients, the mother's milk will supply all the factors, such as nutrients, antibiotics and other bioactives, that the joey needs to grow into a healthy adult wallaby. These factors are controlled by the mother wallaby's genes. Because a cow is also a mammal, it is likely to have similar genes hidden in its genome. Scientists working on this project from the Dairy Cooperative Research Centre and the University of Melbourne can find these similar cow genes by matching them with the relevant wallaby genes. This work will speed up the discovery of bioactives in cow's milk. These tiny compounds can be used in high-value products, such as foods with nutritional benefits, pharmaceuticals or even cosmetics.

Milk on, Milk off

The fur seal, echidna and platypus each have novel lactation strategies controlled by genes that could give useful insights into improving the breeding programs or management of dairy herds. The fur seal, for instance, can 'switch off' lactation while it goes out to sea for up to 25 days to find food, and then switch it 'on' again when it returns to its pup. Imagine if dairy farmers could 'switch off' their cows for the weekend!

Big Mama's milk

High-tech analysis of milk from Big Mama, a five-kilogram echidna in her forties, will help Dairy CRC scientists to find bioactives and the genes responsible for making them. This research will speed up the discovery of bioactives in cow's milk, which may have health and nutritional benefits for humans.

Big Mama lives at the Pelican Lagoon Research and Wildlife Centre on Kangaroo Island, where she is part of a comprehensive echidna research program.

Photo: Rismiller-McKelvey tammar wallabies at University of Melbourne's Wantirna research facility, University of Melbourne.



Oh yeah, how to milk a wallaby...

First, catch your female wallaby and remove its joey to a warm, cosy place. Inject your wallaby with the hormone oxytocin – this prompts its milk to flow. Gently massage the mammary gland, and bingo: wallaby milk.



FURTHER INFORMATION

If you have further questions on genetic modification, visit Biotechnology Australia's website: www.biotechnology.gov.au, or contact the Gene Technology Information Service on 1800 631 276 (free call), fax (03) 9348 2934 or email gtis-australia@unimelb.edu.au. This publication was produced by Biotechnology Australia, the Australian Government's agency for coordinating biotechnology issues, the Gene Technology Information Service and CSIRO's Double Helix Science Club.