Transgenic Animals: Their Benefits To Human Welfare

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Transgenic mice, rats, rabbits, pigs, sheep, and cows have already been created.

A natural protein produced in the milk of transgenic cows like this one kills the bacteria that cause animal mastitis. Source: USDA.

Nowadays, breakthroughs in molecular biology are happening at an unprecedented rate. One of them is the ability to engineer transgenic animals, i.e., animals that carry genes from other species. The technology has already produced transgenic animals such as mice, rats, rabbits, pigs, sheep, and cows. Although there are many ethical issues surrounding transgenesis, this article focuses on the basics of the technology and its applications in agriculture, medicine, and industry.

What is a transgenic animal?

There are various definitions for the term *transgenic animal*. The Federation of European Laboratory Animal Associations defines the term as an animal in which there has been a deliberate modification of its *genome*, the genetic makeup of an organism responsible for inherited characteristics.[5]

A transgenic animal is one whose genome has been changed to carry genes from other species.

The nucleus of all cells in every living organism contains genes made up of DNA. These genes store information that regulates how our bodies form and function. Genes can be altered artificially, so that some characteristics of an animal are changed. For example, an embryo can *have an extra, functioning gene from another source artificially introduced into it, or a gene introduced which can knock out the functioning of another particular gene in the embryo. Animals that have their DNA manipulated in this way are knows as transgenic animals.*[20]

The majority of transgenic animals produced so far are mice, the animal that pioneered the technology. The first successful transgenic animal was a mouse.[6] A few years later, it was followed by rabbits, pigs, sheep, and cattle.[8,14,15,16]

Why are these animals being produced? The two most common reasons are:

Transgenic animals are useful as disease models and producers of substances for human welfare.

- Some transgenic animals are produced for specific economic traits. For example, transgenic cattle were created to produce milk containing particular human proteins, which may help in the treatment of human emphysema.
- Other transgenic animals are produced as disease models (animals genetically manipulated to exhibit disease symptoms so that effective treatment can be studied). For example, Harvard scientists made a major scientific breakthrough when they received a U.S. patent (the company DuPont holds exclusive rights to its use) for a genetically engineered mouse, called OncoMouse® or the Harvard mouse, carrying a gene that promotes the development of various human cancers.[22]

How are transgenic animals produced?

Since the discovery of the molecular structure of DNA by Watson and Crick in 1953, molecular biology research has gained momentum. Molecular biology technology combines techniques and expertise from biochemistry, genetics, cell biology, developmental biology, and microbiology.[2]

Scientists can now produce transgenic animals because, since Watson and Crick's discovery, there have been breakthroughs in:

The insertion of a foreign gene (transgene) into an animal is successful only if the gene is inherited by offspring.
The success rate for transgenesis is very low and successful transgenic animals need to be cloned or mated.

- recombinant DNA (artificially-produced DNA)
- genetic cloning
- analysis of gene expression (the process by which a gene gives rise to a protein)
- genomic mapping

The underlying principle in the production of transgenic animals is the introduction of a foreign gene or genes into an animal (the inserted genes are called transgenes). The foreign genes "must be transmitted through the germ line, so that every cell, including germ cells, of the animal contain the same modified genetic material."[26] (*Germ cells* are cells whose function is to transmit genes to an organism's offspring.)

To date, there are three basic methods of producing transgenic animals:

- DNA microinjection
- Retrovirus-mediated gene transfer
- Embryonic stem cell-mediated gene transfer

Gene transfer by microinjection is the predominant method used to produce transgenic farm animals. Since the insertion of DNA results in a random process, transgenic animals are mated to ensure that their offspring acquire the desired transgene. However, the success rate of producing transgenic animals individually by these methods is very low and it may be more efficient to use cloning techniques to increase their numbers. For example, gene transfer studies revealed that only 0.6% of transgenic pigs were born with a desired gene after 7,000 eggs were injected with a specific transgene.[27]

DNA microinjection is the predominant transgenesis method.

1. DNA Microinjection

The mouse was the first animal to undergo successful gene transfer using DNA microinjection.[6] This method involves:

- transfer of a desired gene construct (of a single gene or a combination of genes that are recombined and then cloned) from another member of the same species or from a different species into the pronucleus of a reproductive cell[19]
- the manipulated cell, which first must be cultured *in vitro* (in a lab, not in a live animal) to develop to a specific embryonic phase, is then transferred to the recipient female

2. Retrovirus-Mediated Gene Transfer

The second method produces chimeras, altered animals with mixed DNA.

A retrovirus is a virus that carries its genetic material in the form of RNA rather than DNA. This method involves:[26]

- retroviruses used as vectors to transfer genetic material into the host cell, resulting in a *chimera*, an organism consisting of tissues or parts of diverse genetic constitution
- chimeras are inbred for as many as 20 generations until homozygous (carrying the desired transgene in every cell) transgenic offspring are born

The method was successfully used in 1974 when a simian virus was inserted into mice embryos, resulting in mice carrying this DNA.[10]

3. Embryonic Stem Cell-Mediated Gene Transfer

The presence of transgenes can be tested at the embryonic state in this third method.

This method involves:[7,19,26]

- isolation of totipotent stem cells (stem cells that can develop into any type of specialized cell) from embryos
- the desired gene is inserted into these cells
- cells containing the desired DNA are incorporated into the host's embryo, resulting in a chimeric animal

Unlike the other two methods, which require live transgenic offspring to test for the presence of the desired transgene, this method allows testing for transgenes at the cell stage.

How do transgenic animals contribute to human welfare?

The benefits of these animals to human welfare can be grouped into areas:

- Agriculture
- Medicine
- Industry

The examples below are not intended to be complete but only to provide a sampling of the benefits.

1. Agricultural Applications

Transgenesis will allow larger herds with specific traits.

a) breeding
Farmers have always used selective breeding to produce animals that exhibit desired traits (e.g., increased milk production, high growth rate).[11,15,17] Traditional breeding is a time-consuming, difficult task. When technology using molecular biology was developed, it became possible to develop traits in animals in a shorter time and with more precision. In addition, it offers the farmer an easy way to increase yields.

Scientists can improve the size of livestock genetically.

b) quality
Transgenic cows exist that produce more milk or milk with less lactose or cholesterol12, pigs and cattle that have more meat on them[8,17], and sheep that grow more wool18. In the past, farmers used growth hormones to spur the development of animals but this technique was problematic, especially since residue of the hormones remained in the animal product.

Disease-resistant livestock is not a reality just yet.

c) disease resistance
Scientists are attempting to produce disease-resistant animals, such as influenza-resistant pigs,

but a very limited number of genes are currently known to be responsible for resistance to diseases in farm animals.[19]

2. Medical Applications

Transplant organs may soon come from transgenic animals.

a) xenotransplantation
Patients die every year for lack of a replacement heart, liver, or kidney. For example, about 5,000 organs are needed each year in the United Kingdom alone.[25] Transgenic pigs may provide the transplant organs needed to alleviate the shortfall.[9] Currently, xenotransplantation is hampered by a pig protein that can cause donor rejection but research is underway to remove the pig protein and replace it with a human protein.[25]

Milk-producing transgenic animals are especially useful for medicines.

b) nutritional supplements and pharmaceuticals
Products such as insulin, growth hormone, and blood anti-clotting factors may soon be or have already been obtained from the milk of transgenic cows, sheep, or goats.[3,12,23] Research is also underway to manufacture milk through transgenesis for treatment of debilitating diseases such as phenylketonuria (PKU), hereditary emphysema, and cystic fibrosis.[3,13,23,25]

In 1997, the first transgenic cow, Rosie, produced human protein-enriched milk at 2.4 grams per litre. This transgenic milk is a more nutritionally balanced product than natural bovine milk and could be given to babies or the elderly with special nutritional or digestive needs.[4,21,23] Rosie's milk contains the human gene alpha-lactalbumin.

A transgenic cow exists that produces a substance to help human red cells grow.

c) human gene therapy
Human gene therapy involves adding a normal copy of a gene (transgene) to the genome of a person carrying defective copies of the gene. The potential for treatments for the 5,000 named genetic diseases is huge and transgenic animals could play a role. For example, the A. I. Virtanen Institute in Finland produced a calf with a gene that makes the substance that promotes the growth of red cells in humans.[24]

Uses in industry include material fabrication and safety tests of chemicals.

3. Industrial Applications

In 2001, two scientists at Nexia Biotechnologies in Canada spliced spider genes into the cells of lactating goats. The goats began to manufacture silk along with their milk and secrete tiny silk strands from their body by the bucketful. By extracting polymer strands from the milk and weaving them into thread, the scientists can create a light, tough, flexible material that could be used in such applications as military uniforms, medical microsutures, and tennis racket strings.[1]

Toxicity-sensitive transgenic animals have been produced for chemical safety testing. Microorganisms have been engineered to produce a wide variety of proteins, which in turn can produce enzymes that can speed up industrial chemical reactions.