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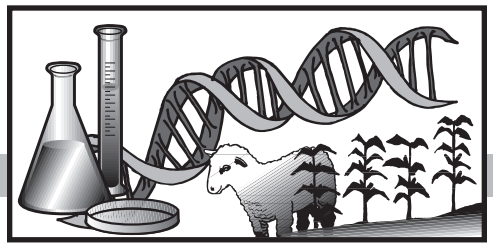

Animal Biotechnology

*Randy Vines**

The tools of biotechnology are being used to enhance animal health and performance, and as a mechanism to use animals for the production of scarce, life-saving pharmaceuticals. The purpose of this publication is to provide basic information about animal biotechnology and give examples of its potential applications.

Biotechnology in Animal Medicines, Vaccines, and Diagnostics

Biotechnology has yielded new and improved medicines for animals that help lower production costs and improve animal well being by fighting diseases caused by bacteria and parasites. For example, scientists have identified a new anti-bacterial compound that may serve as a substitute for using some antibiotics in animals, a practice that has been criticized for contributing to the increased prevalence of drug-resistant bacteria in human infections.

New or enhanced animal vaccines have also been developed through modern biotechnology techniques. Vaccines are now used to prevent diseases including: foot and mouth disease, scours, brucellosis, shipping fever, feline leukemia, rabies, and infections affecting cultivated fish.

Biotechnology has led to the development of rapid test kits to diagnose the health of livestock and companion animals. Some kits are commercially available, but they will have to be low cost and easy to use if they are to be widely accepted.

Biotechnology and Transgenic Animals

Advances in scientific discovery and laboratory techniques in the last half of the twentieth century resulted in the ability to manipulate the deoxyribonucleic acid (DNA) of organisms and gave rise to transgenic animals. The use of transgenic animals may accelerate classical breeding programs and provide a means for the economical production of life-saving pharmaceuticals.

To understand how a transgenic animal is produced, it is necessary to review the basic components and functions of living organisms.

Genes and the Genome

Animals are made of billions of cells all working together. Every cell of the animal has a complete "instruction manual" or genome (pronounced "JEE-nõm") that is inherited from the parents of the animal as a combination of their genomes. The genome resides in the *nucleus* of the cell.

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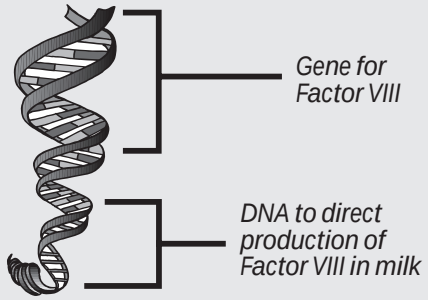
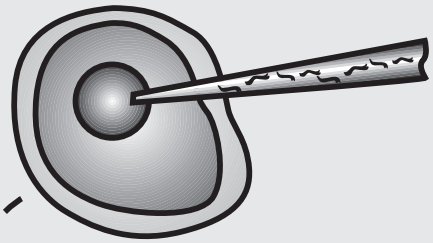
Steps used by Virginia Tech researchers to produce Human Factor VIII in transgenic pigs. Factor VIII is a blood clotting factor that is missing in people afflicted with the bleeding disorder hemophilia A.

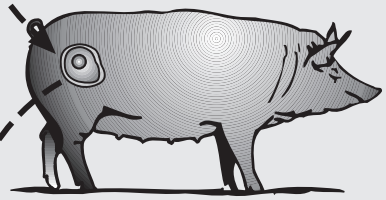
Step 1. Identify and copy the human gene (a particular segment of DNA) for Factor VIII. Combine it with another piece of DNA that will cause Factor VIII to be produced specifically in the pig's milk.



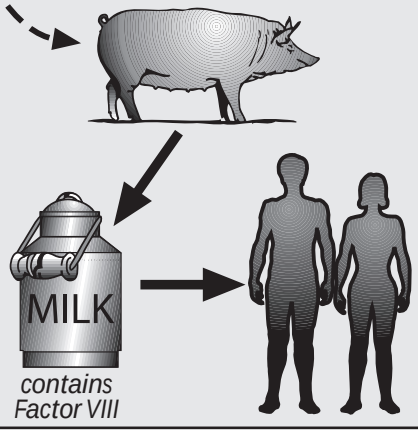
Step 2. Isolate fertilized pig eggs and inject them with the Factor VIII gene.



Step 3. Implant the injected egg into a surrogate mother pig.



Step 4. The transgenic pig is born, when mature it produces Factor VIII in its milk. Factor VIII is purified from the milk and may one day be used to treat people.



Genes are found within the genome and serve as the "words" of the instruction manual. When a cell reads a word (expresses a gene), a specific protein is produced. Proteins give an individual cell, and therefore the animal, its form and function. Genes (words) are written using the four-letter alphabet A, C, G, T. The letters stand for four chemicals called bases, which together compose DNA.

DNA is universal in nature, meaning that the four chemical bases of DNA are the same in all living organisms. Consequently, a gene from one organism can function in another organism.

When a new gene is put into an animal's genome it is said to be *transgenic*. Scientists have also discovered how to genetically modify (GM) when and/or where in an animal a gene is expressed. For example, it is possible to produce new proteins in the milk of a cow and nowhere else in its body.

Making a Transgenic Animal

One way to produce transgenic animals is through a technique called *microinjection*. Once scientists have identified and isolated the piece of DNA comprising the gene to be transferred, it is injected into a fertilized egg of the desired animal using a very small glass needle visualized under a microscope. In approximately one percent of the injected eggs, the gene becomes a new "word" in the egg's "instruction manual" by physically combining with the egg's genome. Ideally, the new gene integrates into the genome before the egg begins to divide. If this occurs, every cell in the animal can contain the new protein and the animal will pass the gene on to its offspring. After injection of the gene, the fertilized egg is implanted into a surrogate mother where it fully develops into a transgenic animal.

Traits Being Introduced Into Animals

Currently, the only routine commercial use of transgenic animals (primarily mice) is in the area of human disease research. One way to characterize the range of genetic modifications that are being considered for use in animals is in the three broad areas of input, output, and value-added traits. Examples of each are described below.

Input traits

An "input" trait helps livestock and dairy **producers** by increasing production efficiency.

Input traits that are being investigated for use in animals:

- Faster, more efficient growth rates
- Increased production of milk or wool
- Resistance to diseases caused by viruses and bacteria

Output traits

An output trait helps **consumers or downstream processors** by enhancing the quality of the animal product.

Output traits that may prove to be beneficial:

- Leaner, more tender beef and pork
- Milk that lacks allergenic proteins, or results in increased amounts of cheese and yogurt

Value-added traits

By adding or modifying genes, animals can function in completely new ways.

- Producing large amounts of therapeutic proteins in animal milk may be an efficient, relatively low cost method to manufacture many proteins used to treat human diseases or proteins that have industrial value.
- Transplanting animal organs into humans, or xenotransplantation, can be made more successful by genetically modifying the organs so that they are not as readily rejected by the human immune system.
- Development of animals that serve as models for human diseases to help scientists better understand prevention and treatment strategies.

Table 1. Proteins with therapeutic and industrial value that have been produced (but not commercialized) in the milk of transgenic animals include:

Protein	Animal	Use
Antithrombin III	Goat	Reduce the amount of blood needed in some surgeries
Factor VIII, Factor IX	Goat, Pig, Sheep	Treatment of hemophilia
CFTR	Sheep	Treatment of cystic fibrosis
Lactoferrin	Cow	Natural antibiotic and used in coronary surgery
Alpha-1-antitrypsin	Sheep	Treatment of cystic fibrosis and emphysema
Lysostaphin	Cow	An anti-bacterial compound that prevents mastitis in cows
Spider silk protein	Goat	Production of ultra-strong, lightweight medical and industrial materials

Risks and Regulation of Transgenic Animals

One concern of transgenic animal technology is the welfare of the animals. Developmental and health abnormalitites have been reported in conjunction with its use; therefore, researchers must take care to minimize animal suffering.

The inadvertant release or escape of transgenic animals (particularly fish) into the wild where they could breed or compete with the natural population is often cited as a potential risk to the environment. The actual risk associated with this will depend on the type of animal and the nature of the genetic modification; however, where appropriate, procedures must be in place to alleviate this concern.

At the Federal level, the Food and Drug Administration, the Department of Agriculture, and the Environmental Protection Agency are required to regulate transgenic animals and their products to ensure that they are safe for public use and the environment. Depending on the nature of the genetic modification, and the proposed use of the resulting animal or product, more than one agency may be involved in the approval process.

Transgenic fish and shellfish

Aquaculture, worth an estimated $46 billion in 1997, produces approximately one-third of all fish and shellfish consumed by humans. As of January 2002, the FDA was considering petitions to allow the commercial use of transgenic salmon and trout with enhanced growth characteristics. In addition, researchers are working with transgenic catfish, carp, tilapia, striped bass, clams, oysters, shrimp, and abalone.

Traits being tested in transgenic fish include:

- Growth rates that are 3-11 times faster with more efficient feed utilization
- Increased tolerance to cold water
- Improved disease resistance

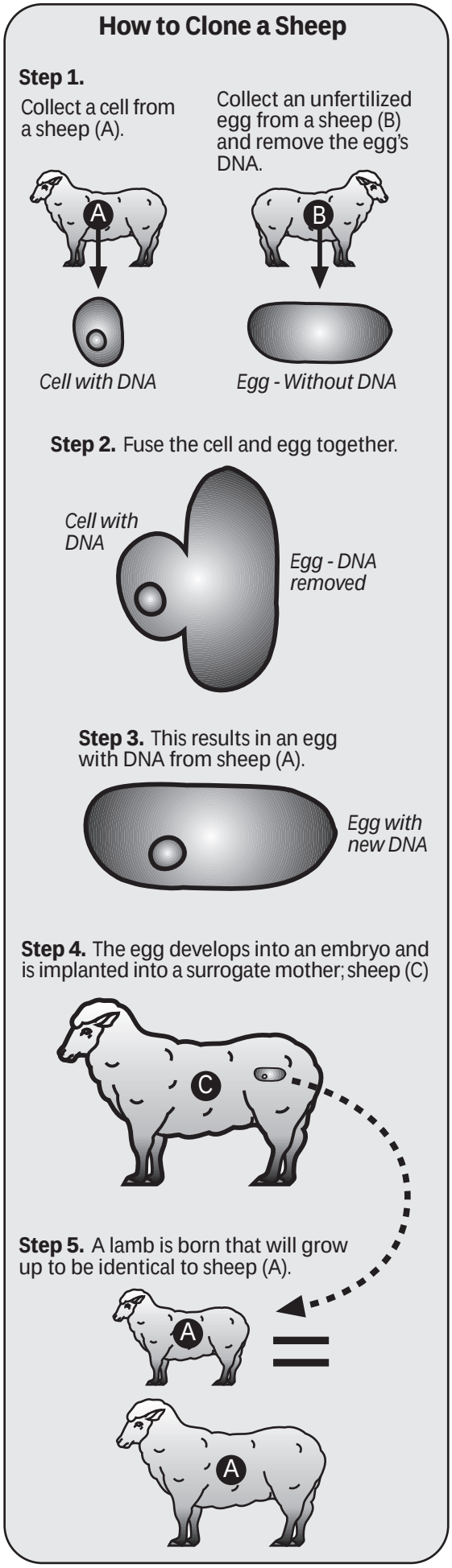
Safety and risk issues associated with transgenic fish:

Issue: Introduction of a protein that is potentially allergenic or toxic to humans

Solution: Extensively test before the FDA grants market approval

Issue: Escape of a transgenic fish into the wild, leading to interbreeding and/or competition with the natural population.

Solution: Restrict cultivation to land-locked facilities or guarantee sterility of transgenic species



Biotechnology and Cloning Animals

Advances in biotechnology have allowed scientists to make genetically identical copies or *clones* of animals. Duplication of an organism's genome occurs naturally when identical twins are born or when a plant is grown from a cutting of another plant. However, the world really took notice of cloning in 1997 when a group of Scottish researchers announced the birth of Dolly the sheep, which had been cloned using a single cell from an adult sheep. Dolly had only one "parent;" her nuclear genome was exactly like her "mother's" instead of being a combination of two parents. Therefore, Dolly could generally be thought of as her mother's identical twin.

To produce Dolly, scientists took an egg from a sheep and removed its nucleus (which contains the genome or instruction manual), rendering it unable to function or develop. Next, they took a cell with an intact genome from a different adult sheep (Dolly's "mother") and fused it to the sheep egg which lacked a genome. The egg, with its new genome, was stimulated to begin developing into an embryo and was implanted into a surrogate sheep where it grew normally, resulting in the birth of Dolly. Dolly later gave birth to normal lambs.

Benefits and Risks of Cloning

Researchers have cloned other mammals including cows, goats, pigs, and mice. However, the overall low rate of successful cloning and frequent occurrence of developmental abnormalities in cloned animals demonstrate the need for further research before cloning will be practical.

It has also been reported that cloned animals may exhibit health problems throughout their life. Cloned animals may age prematurely as Dolly was diagnosed with arthritis at a seemingly young age and cloned mice had a shorter than normal life span. Additionally, it was demonstrated that cloned mice were both larger in size and heavier than a control group of non-cloned mice.

If advances in animal cloning technology were to overcome the current obstacles, the most obvious benefit would be the ability of a farmer to have a herd of superior performing animals in one generation. Breeding companies could sell cloned embryos in a manner similar to the way in which semen is currently marketed. A potential drawback of this practice would be the loss of genetic diversity in livestock herds, but this could be avoided by limiting the number of cloned embryos of a given animal that were sold.

It has also been proposed that cloning could be used to increase the population of animals in an endangered species. The mouflon sheep, which is a wild Mediterranean sheep with less than 1000 animals remaining, was successfully cloned. Additionally, scientists are attempting to clone an endangered wild Asian ox, called the guar (the first cloned guar died of an intestinal illness shortly after birth) and possibly the giant Panda. Although possible, a recovering population of cloned animals would be hindered by a lack of genetic diversity and would not address the larger issue of how the animal became endangered.