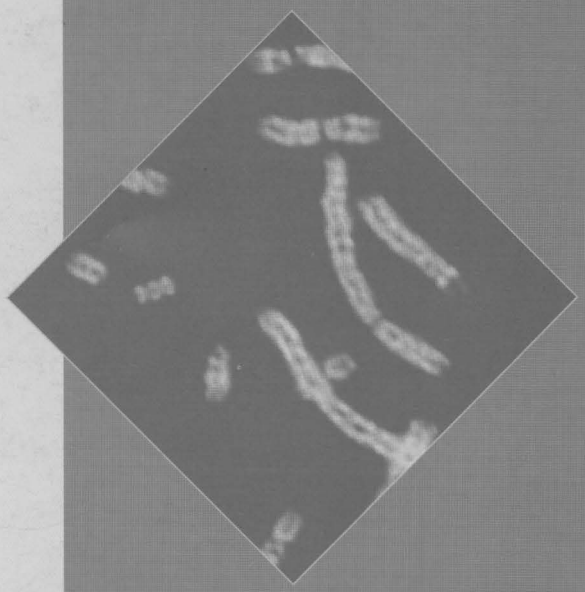
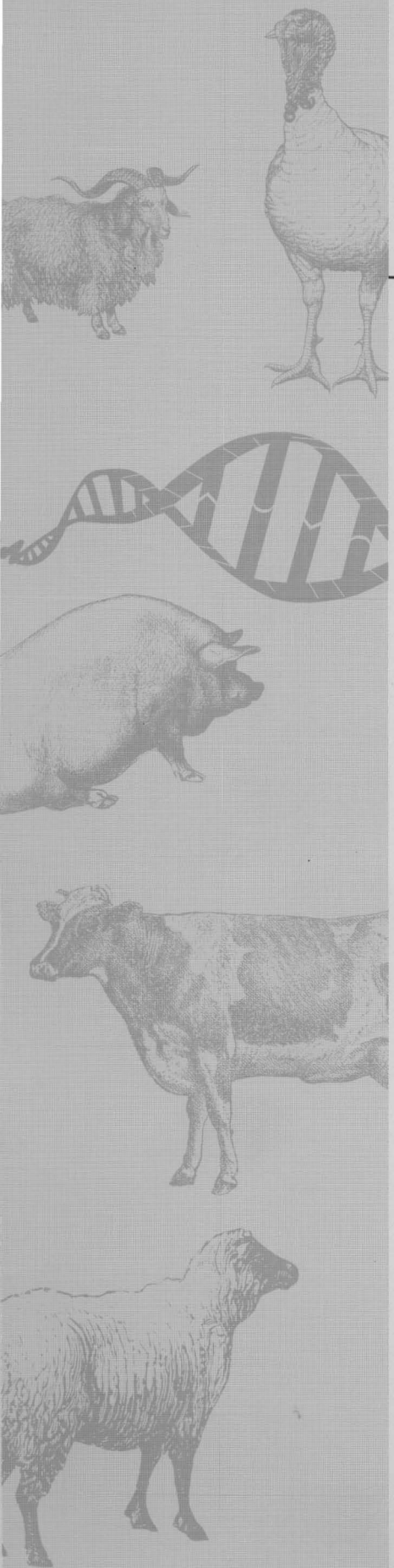
# Animals By Design



## A Primer on the Tools of Modern Biotechnology

UNIVERSITY OF MINNESOTA

**Minnesota Report 244–1998**
**Minnesota Agricultural Experiment Station**




**Credits:**

Lawrence B. Schook, director, Food Animal Biotechnology Center, and associate dean for research and graduate programs, University of Minnesota College of Veterinary Medicine

Mary Hoff, writer

James Kiehne, designer

Larry Etkin, product manager and senior editor for the Minnesota Agricultural Experiment Station, University of Minnesota

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Ronald Phillips, regents' professor, Department of Agronomy and Plant Genetics, University of Minnesota

Abel Ponce de León, head, Department of Animal Science, and codirector, Food Animal Biotechnology Center, University of Minnesota

Anuradha Subramanian, professor, Department of Biosystems and Agricultural Engineering, University of Minnesota

Jeremy Taylor, professor, Department of Animal Science, Texas A&M University—College Station

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# Contents


| | | |
|---|---|---|
| Foreword | **Opportunity and Challenge** | . . . . . 3 |
| Chapter One | **A Bit on the Basics**<br>*a user-friendly overview of genetics* | . . . . . 4 |
| Chapter Two | **Genome Mapping**<br>*behind the scenes in the theater of life* | . . . . . 8 |
| Chapter Three | **Mapping Applications**<br>*expediting breed improvement* | . . . . . 14 |
| Chapter Four | **Genetic Engineering**<br>*genes on the move* | . . . . . 18 |
| Chapter Five | **Improving Conventional Products**<br>*genetic engineering and animal agriculture* | . . . . . 20 |
| Chapter Six | **Medicines and More**<br>*engineering for nontraditional products* | . . . . . 22 |
| Chapter Seven | **Beyond Biology**<br>*social and ethical issues* | . . . . . 24 |
| | **Glossary** | . . . . . 26 |
| | **For Further Information** | . . . . . 28 |

# *new genetics meets animal production*

*Human dependence on animals traces back to prehistoric times. With the advent of domestication, we began to encourage the propagation of animals that best met our needs. The specialized breeds that resulted provide high-quality food, labor, shelter, companionship, clothing, medicine, and more.*

*Many food animals today are far more productive than their wild counterparts, thanks in part to selective breeding.*

# Opportunity and Challenge

As long as humans have existed, we have depended on animals to meet our most basic needs—to nourish and clothe us, carry our loads, herd our livestock, and be our companions. As we refined this relationship through domestication, we began to actively alter animals by preferentially breeding those that provided more milk, finer wool, cuter puppies, and so on. Individuals that best met our desires became the seedstock for the next generation.

Today, ***genomics***—the study of the molecular material that determines heredity—is giving us new, far more efficient ways of shaping animals to meet our needs. Our ancestors tamed wild beasts; today we are taming genes, selectively retaining those that serve our needs, culling those that work against us, bringing in new ones to meet new needs. Improvements that once would have taken decades can now be accomplished in a few years.

From a food production perspective, the timing couldn't be better. With continuing growth in both global population and environmental concerns, farmers around the world are being pushed to produce more food, more efficiently, while maintaining land, water, and air quality. Genetic technology can be a valuable tool to help us meet this complex challenge of feeding the world while being stewards of the environment.

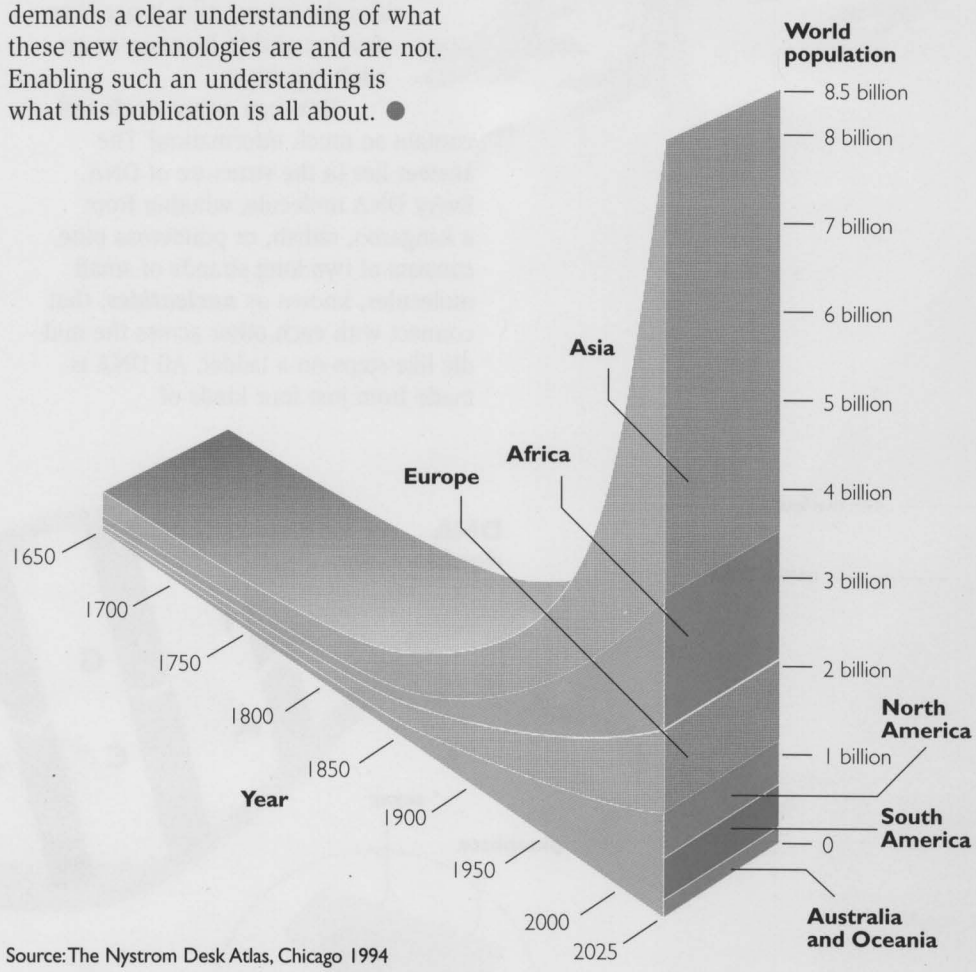
Improving food production is not the only benefit. We are also applying our growing ability to work with genetic material by producing better wool for our clothing, developing new sources of life-saving medicines, and improving the qualities of companion animals. We are even advancing the potential for xenotransplantation—the use of animal organs and tissues in treating human diseases.

This new frontier is exciting. It also is sobering. Our ability to manipulate genes has the potential to influence our future as dramatically as domestication altered the course of human history long ago—both in ways we desire and in ways we might not.

Today's challenge is to clearly delineate the advantages and disadvantages of both applying and not applying these new capabilities, then make rational and informed choices about what is best for ourselves, our children, and generations to come. That is a job for every concerned citizen. It is a job that demands a clear understanding of what these new technologies are and are not. Enabling such an understanding is what this publication is all about. ●

**genomics:** *the study of the total molecular material that determines heredity.*

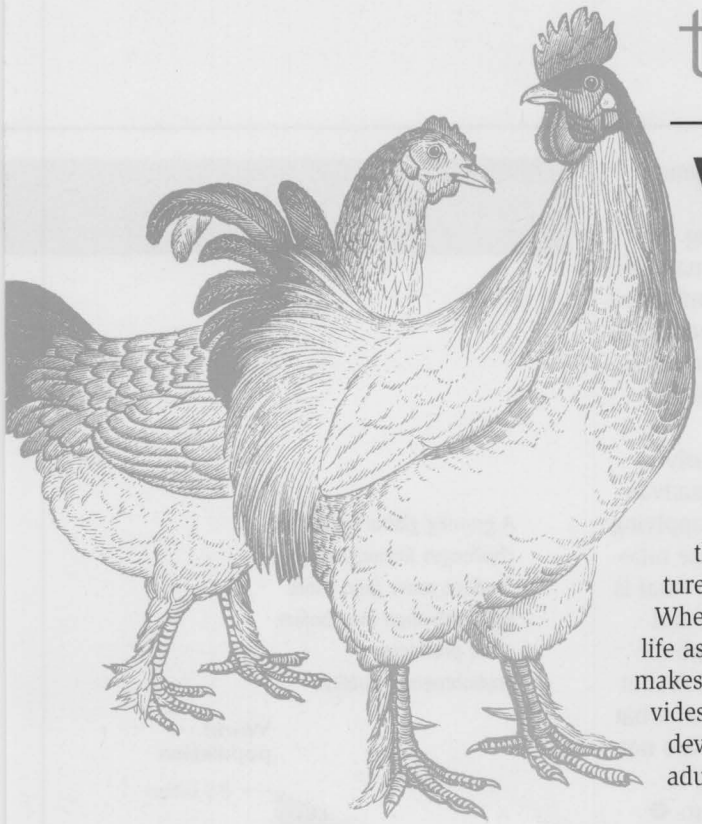
*A growing global population challenges farmers to produce more food, more efficiently than ever before while protecting environmental quality.*




Source: The Nystrom Desk Atlas, Chicago 1994

# A Bit on the Basics

*a user-friendly overview of genetics*



What makes a chicken a chicken instead of a fungus? Why does one cow produce more and better milk than an identically managed neighbor? It all boils down to ***DNA.***

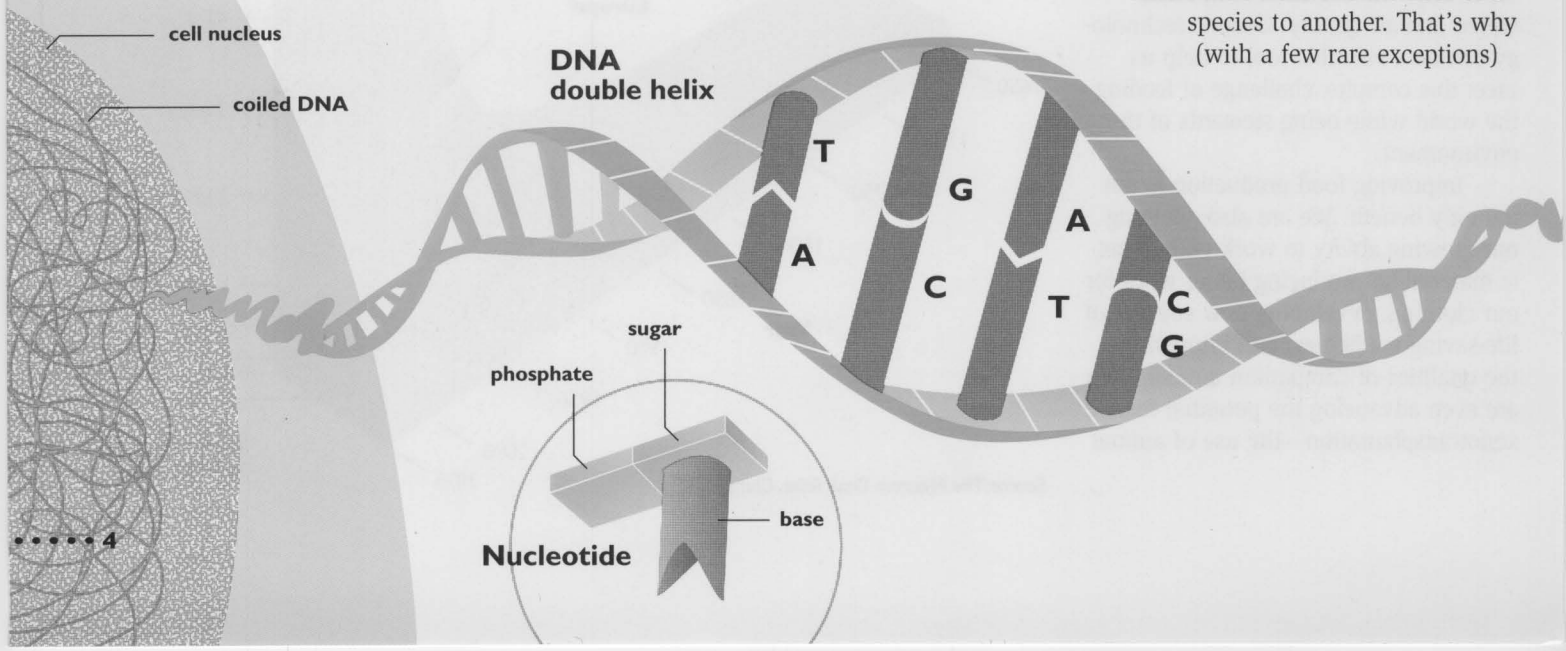
DNA is a rope-like megamolecule found in the cells of living things. In animals, it is nestled in the nuclei of its cells in structures called ***chromosomes.*** When a plant or animal begins life as a single cell, the DNA that makes up its chromosomes provides the information it needs to develop and to function as an adult organism.

How can a tiny single cell contain so much information? The answer lies in the structure of DNA. Every DNA molecule, whether from a kangaroo, radish, or ponderosa pine, consists of two long strands of small molecules, known as ***nucleotides,*** that connect with each other across the middle like steps on a ladder. All DNA is made from just four kinds of nucleotides, which in turn are made from a sugar, a phosphate molecule, and one of four bases: adenine, thymine, cytosine, and guanine. These are most often identified by the shorthand labels A, T, C, and G.

It is the specific order in which these nucleotides appear along the DNA strands that provides the information an organism needs to develop and function. In stretches of DNA known as ***genes,*** the arrangement of the nucleotides creates a code. Just as a bar code on the back of a can of beans describes a specific type of beans, the order of the nucleotides within each gene describes a specific type of protein. Cells use these descriptions to manufacture the described proteins. The proteins, in turn, tell the cells what they will become (eye, skin, liver, and so forth) and direct their activities—how they grow, what they do, and how they work with other cells to produce the blend of structure and function that makes the organism what it is.

## Many Forms

For most of the length of each chromosome, the order of nucleotides differs little from one member of a species to another. That's why (with a few rare exceptions)



# Recipe for Life

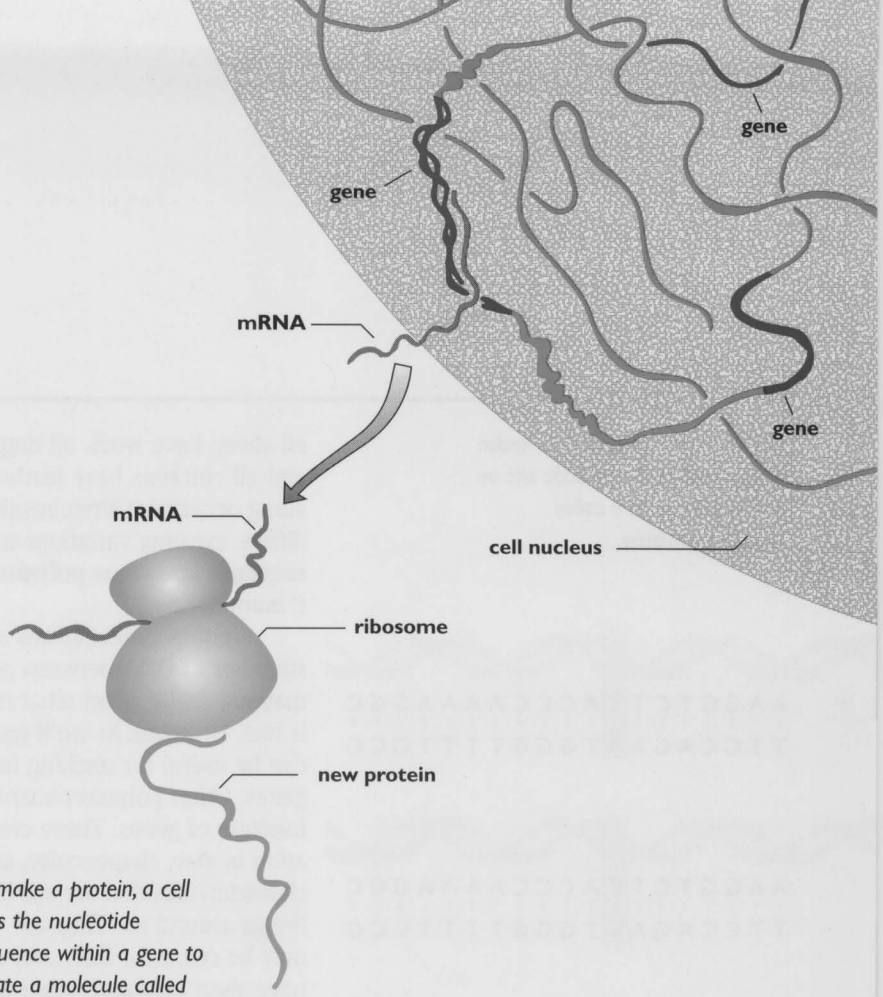
Where does a fertilized egg get the information it needs to develop into a living, breathing animal?

When an animal is conceived from sperm and egg, it receives a set of structures, called chromosomes, from each parent. Chromosomes contain DNA, which in turn is made up of chains of nucleotides, four similar types of molecules represented in biochemical shorthand as the letters A, T, C, and G.

In certain stretches of the DNA, known as genes, the order in which nucleotides appear creates a "recipe" for concocting a specific protein. Proteins, in turn, guide the cellular activity that creates the blend of form and function we know as life. If you think of an animal as a banquet table set with a vast smorgasbord of traits, you can liken the DNA to a cookbook. This cookbook is constantly being consulted for instructions on how to combine the molecules in cells into a tasty dish to add to the spread.

As an organism grows, the entire DNA cookbook is copied and passed to each new cell. However, most cells use only some of the recipes. Skin cells activate DNA used to make skin-related proteins, nerve cells activate DNA used to make nerve-related proteins, and so on.

The amount of information stored in DNA varies. A bacterial cell contains about 1,000 to 5,000 gene-recipes. The genetic cookbook of a cow or a human, on the other hand, can hold 100,000 or more.




*To make a protein, a cell uses the nucleotide sequence within a gene to create a molecule called* ***mRNA.*** *This molecule then moves from the nucleus to another structure, known as a* ***ribosome,*** *where it is used as a template for the manufacture of a protein from amino acids.*

*The nuclei of animal cells contain chromosomes, spaghetti-like structures made of long molecules known as DNA. DNA in turn is constructed from a combination of four types of smaller molecules, called nucleotides. The order in which nucleotides (known in biochemical shorthand as A, T, C, and G) appear along the DNA creates recipes for making the organism what it is.*

**chromosomes:** *structures found within the nuclei of cells that contain the organism's genetic material.*

**DNA (deoxyribonucleic acid):** *a large polymeric molecule that is made up of nucleotides and other components and that contains the information needed to define structure and function of an organism. DNA is the main nonprotein component of chromosomes.*

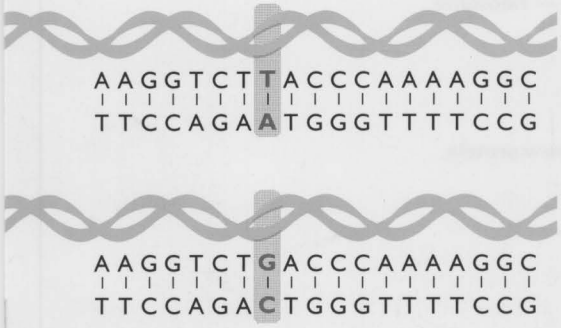
**gene:** *a stretch of DNA that contains the information needed to create a protein.*

**mRNA:** *a molecule that carries information from genes to ribosomes to form proteins.*

**nucleotide:** *a piece of DNA that includes one of the bases that makes up the genetic code along with the corresponding bit of DNA backbone.*

**ribosome:** *a structure within a cell that makes proteins.*

*Variations in the amount or order of nucleotides at a specific site on a chromosome are called* ***polymorphisms.***




all sheep have wool, all dogs have tails, and all chickens have feathers. But along occasional stretches the pattern differs, creating variations in nucleotide sequence known as ***polymorphisms*** ("many forms").

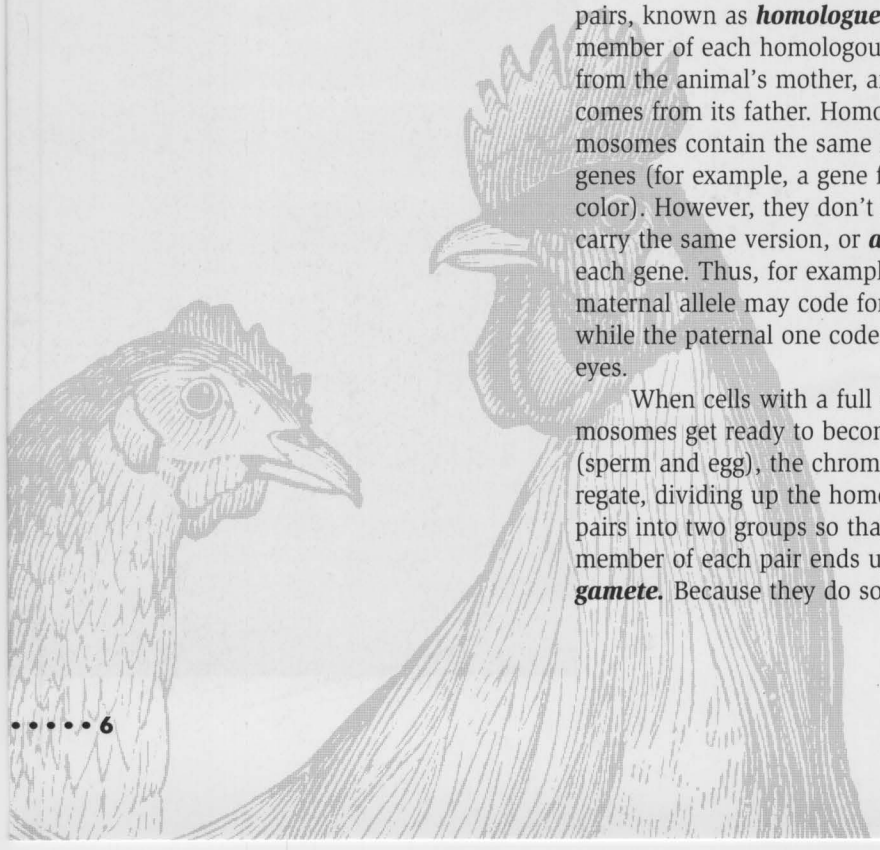
Some polymorphisms occur in the stretches of DNA between genes. These may not really affect what the organism is like. However, as we'll see later, they can be useful for tracking important genes. Other polymorphisms affect the function of genes. These create the variation in size, shape, color, and other characteristics that we see in the living things around us. They are why wool may be coarse or fine, why some dogs have short tails and others have long ones, and why one chicken has white feathers while another has brown.

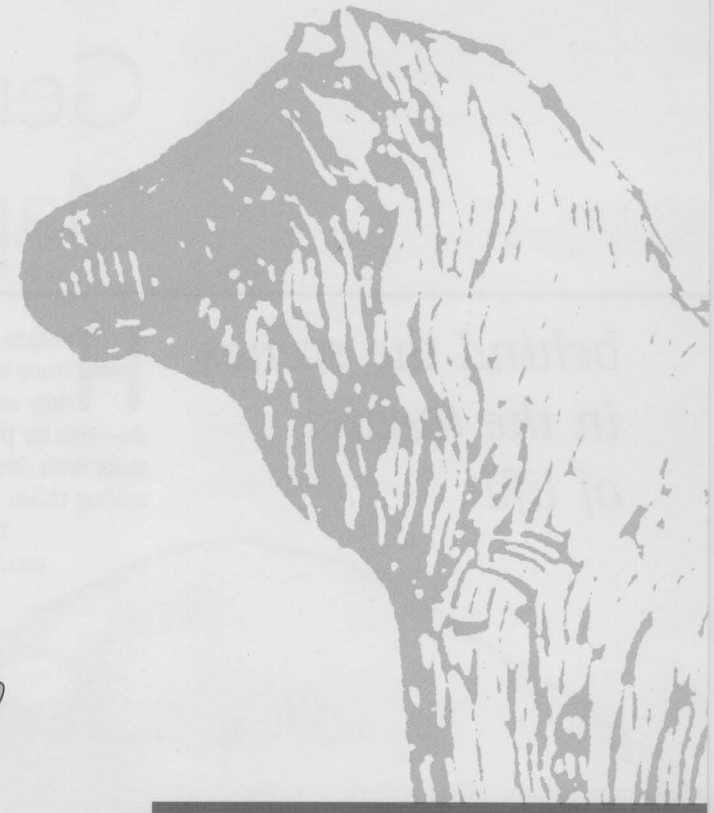
## Passing It On

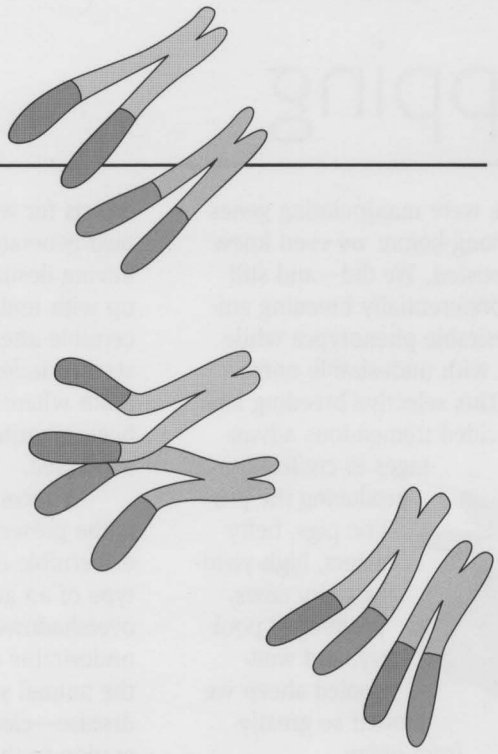
Different species have different numbers of chromosomes. But in all animals, the chromosomes come in pairs, known as ***homologues.*** One member of each homologous pair comes from the animal's mother, and the other comes from its father. Homologous chromosomes contain the same kinds of genes (for example, a gene for eye color). However, they don't necessarily carry the same version, or ***allele,*** of each gene. Thus, for example, the maternal allele may code for blue eyes, while the paternal one codes for brown eyes.

When cells with a full set of chromosomes get ready to become gametes (sperm and egg), the chromosomes segregate, dividing up the homologous pairs into two groups so that only one member of each pair ends up in each ***gamete.*** Because they do so randomly, genes on different chromosomes (for example, a blue-eyed gene on one chromosome and a gene for big feet on another) have only a 50-50 chance of ending up in the same gamete. DNA bits on the same chromosome have a much higher chance of ending up in the same gamete. (That's why, for example, red hair and freckles are often inherited together.) However, it's not a 100 percent chance. The link between two genes on the same chromosome can be broken by a process called ***crossing over,*** or ***recombination.*** In this process, homologous chromosomes exchange segments as they divide into two groups to form gametes (see illustration, page 7). Because of crossing over, genes that started out on the same chromosome can be inherited separately from each other, and gametes rarely contain chromosomes exactly identical to those found in the cells of the parent animal.

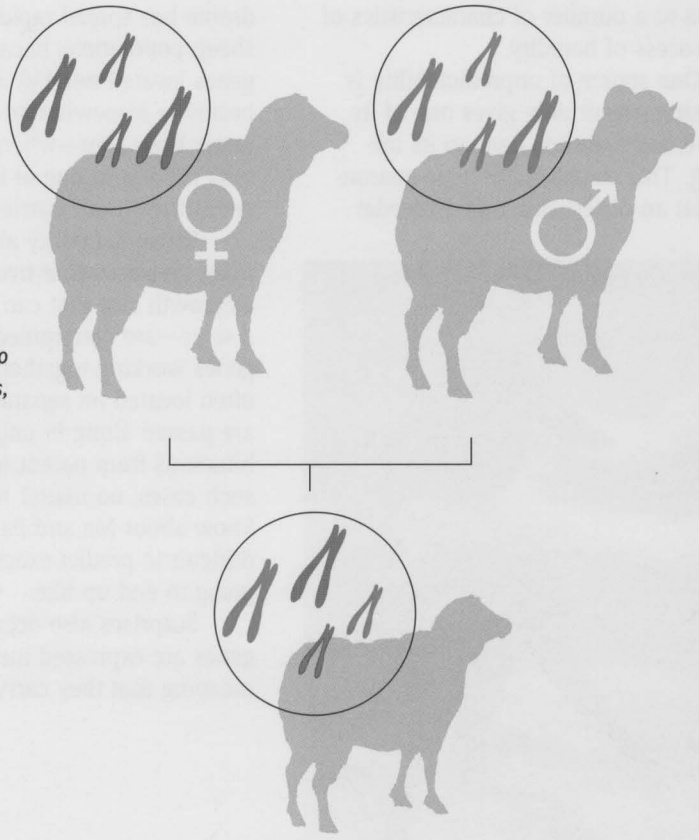
Which of the two alleles of each gene brought together by sperm and egg determines the ***phenotype***—observable characteristics—of the new organism? That depends. If the animal is ***homozygous*** for the trait—that is, both alleles are identical—it doesn't really matter which does the work because the results are the same. But if the animal is ***heterozygous***—the alleles are different—a couple of different things could happen. For some genes, both alleles contribute to the outcome. In other instances one allele determines phenotype, while the other simply hangs out behind the scenes. These "invisible" alleles can serve up huge surprises when they are passed along to future generations, pair up with identical alleles, and produce a phenotype unlike that of either parent. ●







*As chromosomes sort themselves out into the two sets that form sperm or egg, they often exchange bits of DNA in a process called crossing over or recombination. Pieces of DNA are considered "linked" if they are so close that they are highly unlikely to be separated in this way.*



*Every animal has two sets of chromosomes, one from its mother and one from its father.*

**alleles:** *alternative forms of the same gene on two chromosomes that determine the expression of a trait (e.g., eye color or resistance to a particular disease).*

**crossing over:** *a process in which homologous chromosomes exchange sections during the process of creating gametes.*

**gametes:** *the cells that carry hereditary material from one generation to the next (sperm and egg).*

**heterozygous:** *having two different alleles for a particular gene.*

**homologues:** *the pairs of chromosomes that carry information for the same types of traits; one of each pair is inherited from the mother and the other from the father.*

**homozygous:** *having two identical alleles for a particular gene.*

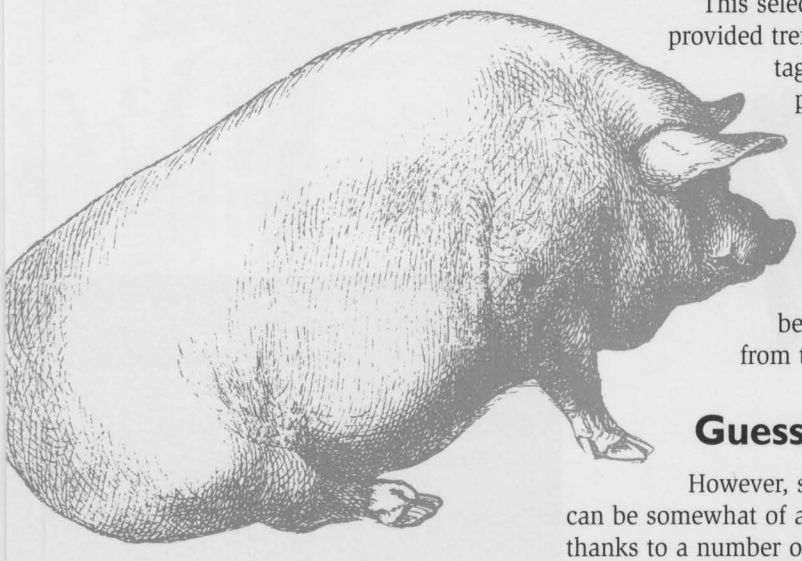
**phenotype:** *the observable characteristics of an organism.*

**polymorphisms:** *stretches of DNA found in the same relative location on a chromosome but differing in the amount or order of nucleotides.*

**recombination:** *exchange of alleles at two heterozygous loci. This is a result of crossover but does not reflect an even number of crossovers.*

# Genome Mapping

## *behind the scenes in the theater of life*



*Selective breeding has produced the prolific pigs and other animals we benefit from today.*

Humans were manipulating genes since long before we even knew they existed. We did—and still do—this by preferentially breeding animals with desirable phenotypes while culling those with undesirable ones.

This selective breeding has provided tremendous advantages to civilization, producing the prolific pigs, hefty steers, high-yielding dairy cows, productive poultry, and well-wooled sheep we benefit so greatly from today.

### Guessing Game

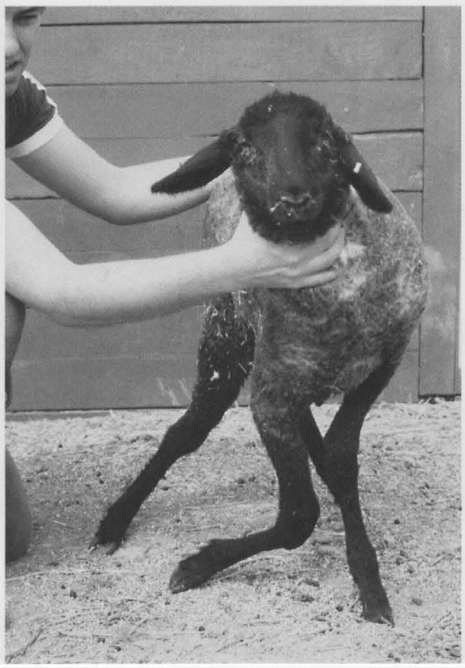
However, selective breeding can be somewhat of a guessing game, thanks to a number of characteristics of the process of heredity.

One source of unpredictability is that each parent only gives one of its two versions of each gene to its offspring. This means there is no guarantee that an observable trait a breeder selects for will get passed along to the next generation. An animal from parents having desirable characteristics may end up with undesirable traits, only discernible after someone has made a substantial investment in raising it to the point where the desirable trait, had it been inherited, would have been expressed.

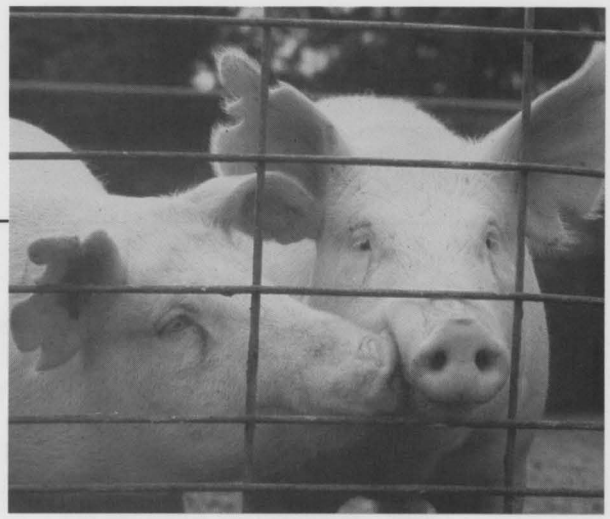
A second source of unpredictability is the presence of alleles that make no discernible contribution to the phenotype of an animal because they are overshadowed by another allele. An undesirable allele—say, one that makes the animal susceptible to a particular disease—can slip quietly from one generation to the next without anyone's knowledge until it is paired up with another of its kind and the trait is expressed. Worse yet, breeders might inadvertently select for it. For example, a bone disorder called spider lamb syndrome has spread rapidly through some sheep populations because the gene (or genes located nearby) appears to bestow a somewhat desirable trait—larger body size—when this allele is only present in one of the two sets of genes the animal carries.

Unpredictability also arises because many ***quantitative traits***—traits such as growth rate that can be measured on a scale—are determined by a number of genes working together. These genes, often located on separate chromosomes, are passed along in unpredictable combinations from parent to offspring. In such cases, no matter how much you know about Ma and Pa, it's extremely difficult to predict exactly what Junior is going to end up like.

Surprises also occur because some genes are expressed incompletely, meaning that they carry more informa-



*Selective breeding can backfire when an allele that causes disease is present on both homologous chromosomes even as it provides a benefit if present on only one. Spider lamb syndrome, an inherited bone disorder that is expressed in animals that have two copies of the detrimental allele, has spread through sheep populations because animals with only one such allele tend to grow bigger than average.*

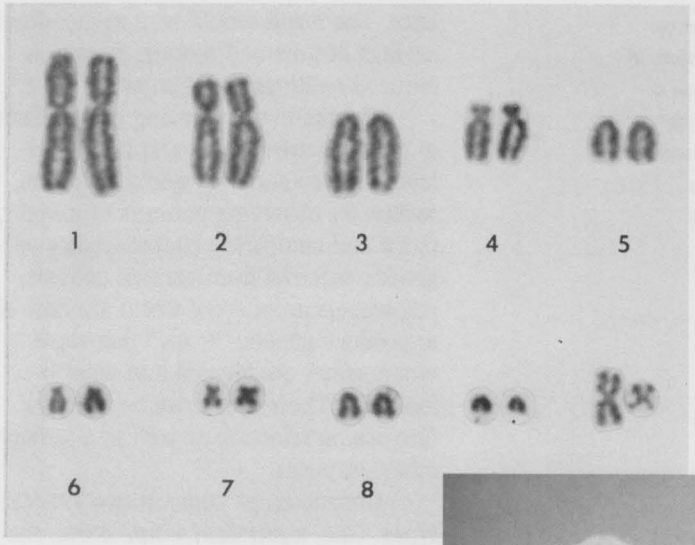


*To breed or not to breed? That is a question agricultural livestock producers routinely face as they work to build a herd or flock with the best possible production characteristics. A particular pig may have parents with genes that promote fast growth or good meat quality. But whether it has inherited those genes—and so should be used as seedstock for future generations—is often anybody's guess.*

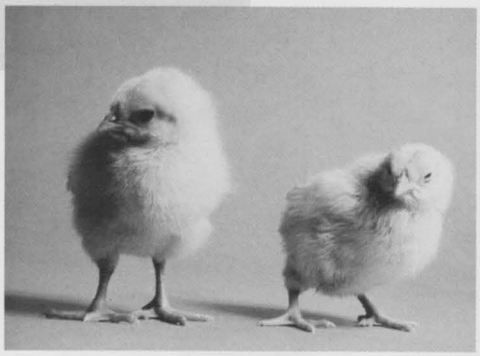
tion than actually shows in a given organism. The suppressed information can be expressed after it has been passed along to the next generation. And some traits are not expressed at all in some genders, even though they are coded for by the genes. For example, bulls may carry an allele for high milk quality, and roosters may carry an allele for prolific egg-laying, but neither will express it.

Another limitation to conventional selective breeding occurs because genes are strung together on chromosomes and tend to be inherited in batches. Occasionally, genes that are near each other separate through the process of crossing over (see Chapter One). However, genes that are close together rarely are separated by crossing over. If one gene is desirable and the other is undesirable, then problems can arise as both are inherited together. For example, researchers suspect that a disease known as porcine stress syndrome (PSS) has become more common in swine because the gene that controls PSS is tightly linked to others that confer desirable meat characteristics and so has been selected for by producers.

For animals in the wild, these pull-a-rabbit-out-of-a-hat variations on the theme of heredity provide a valuable source of diversity that allows species to adapt to alterations in the environment around them. But for domestic animals, they pepper even the most elaborate and foresightful breed improvement plans with inefficiences and waste. Though we have done, and can do, much to promote desirable traits, at times the outcome of selective breeding efforts seems frustratingly dictated by blind luck.

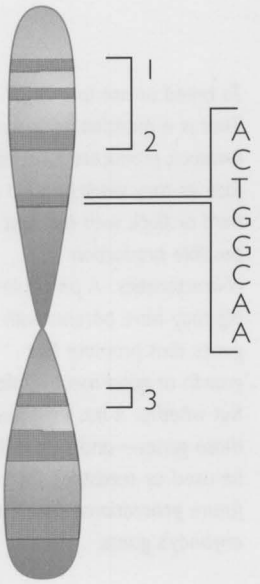



*With conventional breeding, we make assumptions about an animal's genetic makeup based on* ***phenotype,*** *or outward appearance. Genetic improvement would be far more efficient if we could instead select animals based directly on their* ***genotype****—the genes actually carried within their cells.*



**genotype:** *the set of genes found within an organism's cells.*

**quantitative traits:** *phenotypic characteristics that can be objectively quantified (e.g., milk or egg production).*




*A physical map can be as general as a rough picture of the location of genes on a chromosome (left), or as specific as the actual order of nucleotides along a section of DNA (right).*

## Managing Genes

Imagine, however, if instead of selecting on the basis of phenotype, we could tunnel down into the core of an animal's cells, view its genetic makeup, and then do our selecting on that basis. We could become far more efficient "gene managers," preferentially allocating our resources to animals that best meet producer and consumer needs based on clear and accurate knowledge of what's really there, rather than on the fuzzy reflection created by the animal's outward appearance. The result would be a tremendous savings of time and money, as well as reduced environmental impacts.

Thanks to our growing understanding of genes at the cellular and molecular level, this scenario is rapidly becoming reality. By observing patterns of inheritance and comparing characteristics of genetic material from various animals, researchers around the world are now able to produce genetic "maps" that show where genes are located and what they look like. These maps can be used for fine-tuning selection as well as a variety of other purposes.

Genetic maps come in two general types. One, a ***physical map,*** shows the actual location of genes—or even individual nucleotides—along an animal's chromosomes. The other, a ***linkage map,*** identifies the location of genes relative to other genes or to easily identified noncoding bits of DNA. Together these maps provide precisely the information breeders have long sought—knowledge of whether specific animals carry the genetic information for specific traits that is independent of whether the traits are phenotypically expressed.

## Physical Maps

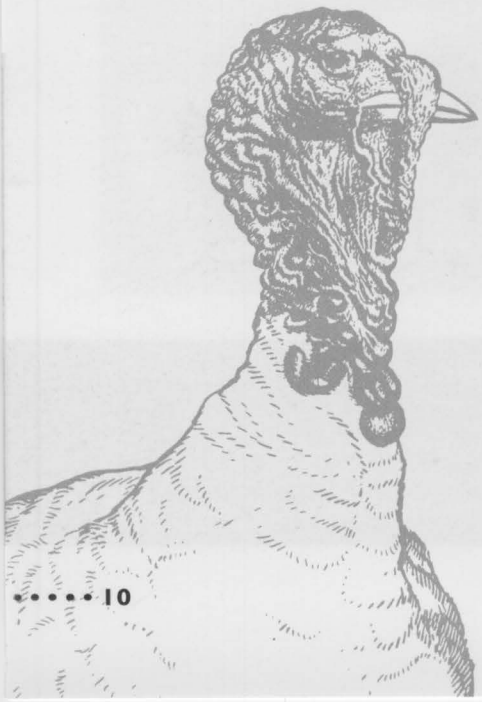
A physical map is a picture of the genome in the same way that a road map is a picture of a city, state, or country. It can have a variety of degrees of resolution, just as a road map might show Paris's every street and alley while a map of France would show the whole city as a single black dot. At the most detailed level, it is an actual description of the lineup of nucleotides along the DNA molecule.

## Sequencing DNA

***Sequencing*** DNA—determining the exact order of bases in a piece of DNA—involves several steps. First, researchers use chemical processes to separate the DNA they are interested in from the other molecules found in animal cells. Then they make millions of copies of it with a technique known as ***polymerase chain reaction,*** or ***PCR.*** Next, these pieces are prepared for sequencing by making sure that no unnecessary DNA is present.

Today's automated DNA sequencers use chain terminating chemistry involving a set of fluorescently labeled nucleotides that have been modified so that when a DNA-building enzyme tries to incorporate them into a chain under construction, the DNA-building process halts. These modified, labeled nucleotides are added to a sequencing reaction mixture along with other nucleotides, the DNA to be sequenced, a primer, and the DNA-building enzyme.

The DNA-building enzyme tries to make new DNA molecules using the target DNA as a template, and the



## The Copy Machine

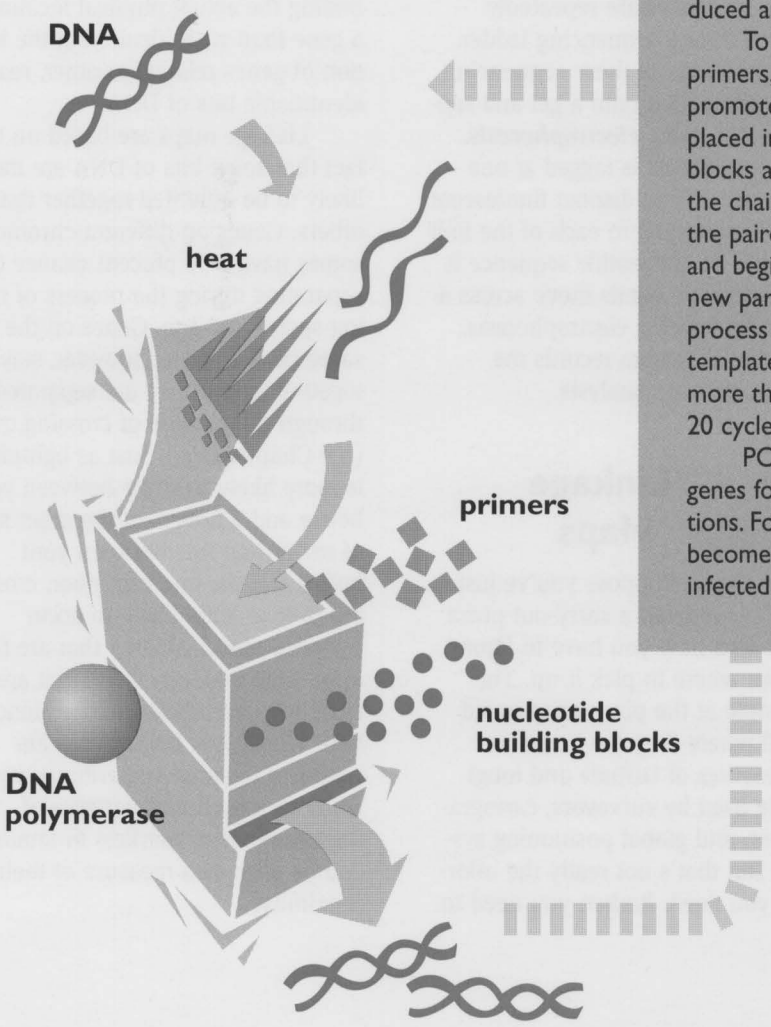
One requirement for working with genes or other bits of DNA is the ability to make a large number of copies of them. In the early days of genetic engineering, copies were made by inserting the DNA into bacteria, waiting for the bacteria to make millions of copies of themselves and their DNA passenger, then extracting the copies. The process was slow and cumbersome.

In 1983, a molecular biologist had a flash of insight: Why not harness the power of the enzyme cells use naturally to make copies of DNA? The refinement of this brainstorm, known as polymerase chain reaction, or PCR, introduced an exciting new era for genetic manipulation.

To use PCR, researchers make molecules, called primers, that bind to the ends of the DNA of interest and promote duplication of that sequence. The primers are placed in solution along with lots of loose DNA building blocks and DNA polymerase, the enzyme that jump-starts the chain-building reaction. The solution is heated, causing the paired DNA strands to separate. The primer moves in and begins the process of adding nucleotides to create a new partner strand. Then the solution is reheated and the process repeated. Because the new DNA is also used as a template, the amount of DNA grows exponentially, yielding more than a million copies of each DNA template in only 20 cycles of the process.

PCR is used for more than just creating copies of genes for research. It also has a variety of practical applications. For instance, in food animal medicine PCR has become valuable for determining whether an animal is infected with a particular disease organism.

### The PCR copy machine




**linkage map:** *a way of describing genetic material according to the relative location of genes and other bits of DNA.*

**PCR (polymerase chain reaction):** *a chemical process used to rapidly make large numbers of copies of DNA segments.*

**physical map:** *a way of describing genetic material according to the actual physical structure of DNA.*

**sequence:** *to identify the order in which nucleotides appear on a particular stretch of DNA.*

**THE SEQUENCING PROCESS**

**Purify DNA**

▼

**Amplify DNA by PCR**

▼

**Prepare Sequencing Template**

▼

**Perform Fluorescent Sequencing Reaction**

▼

**Electrophorese Dye-labeled Samples**

▼

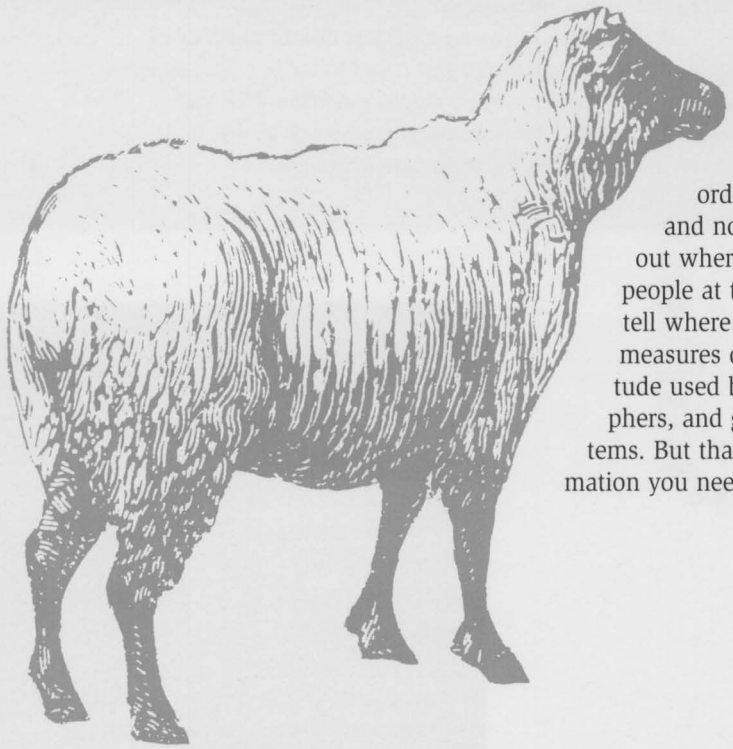
**Analyze Data**

▼

**Compare Data**

normal and modified nucleotides as building blocks. Because the process halts every time a modified nucleotide is used, the result is a family of DNA molecules, each one nucleotide longer than the previous, like rungs on a ladder. Actual sequencing reactions are usually performed by a thermal cycle sequencing process, in which a few initial target molecules are repeatedly used to generate a sequencing ladder.

The products of these sequencing reactions are loaded onto a gel and separated by size using ***electrophoresis.*** Since each molecule is tagged at one end with one of four distinct fluorescent labels, corresponding to each of the four nucleotides, the nucleotide sequence is determined as the bands move across a small window during electrophoresis, where a digital camera records the image for computer analysis.

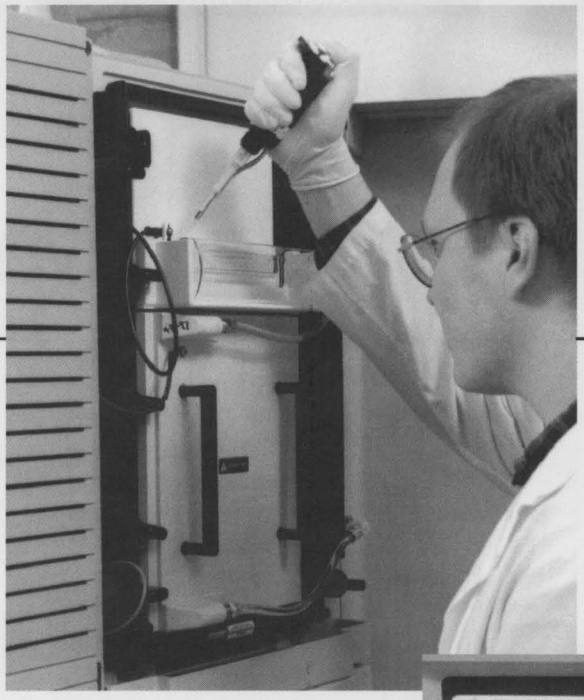


## Linkage Maps

Suppose you've just ordered a carry-out pizza and now you have to figure out where to pick it up. The people at the pizza shop could tell where they are based on measures of latitude and longitude used by surveyors, cartographers, and global positioning systems. But that's not really the information you need. Rather, you need to find out where the pizza place is relative to other places you already know—for example, three blocks past a prominent intersection or a block from the post office.

Pinpointing a location using other known entities as landmarks is what ***linkage mapping*** is all about. Linkage maps have less to do with finding the actual physical location of a gene than with identifying the location of genes relative to other, readily identifiable bits of DNA.

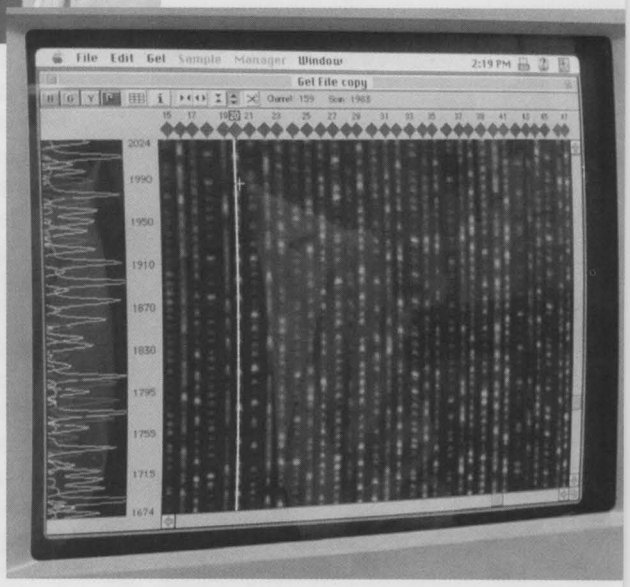
Linkage maps are based on the fact that some bits of DNA are more likely to be inherited together than others. Genes on different chromosomes have a 50 percent chance of separating during the process of making sperm and egg. Genes on the same chromosome, however, stay together unless they are separated through the process of crossing over (see Chapter One). Just as lightning is more likely to strike between your house and a house on the other side of town than it is between your house and the one next door, crossing over is more likely to occur between pieces of DNA that are far apart than between those that are close together. Thus, the frequency with which two DNA pieces are inherited together (determined by a study of inheritance patterns of known genes or markers in families) can be used as a measure of their proximity.



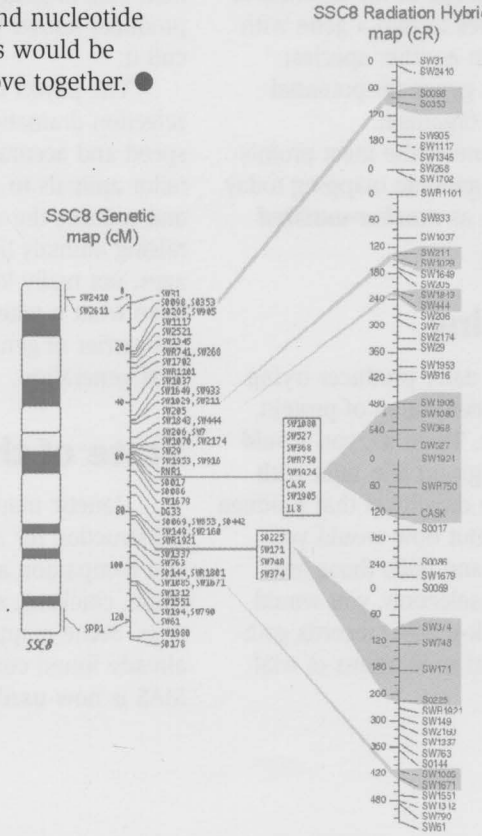
## Genetic Distance

Distances on linkage maps are measured in ***centiMorgans*** (cM). A centiMorgan describes how likely it is that two DNA bits will be inherited together. Just as you can describe the distance to the pizza parlor in blocks (even though you don't know how long a block is), geneticists can describe the distance between points in the genome in centiMorgans, even without a clue as to the actual physical distance.

Bits of DNA separated by a linkage distance of 1 cM are said to have one chance in 100 to be separated and end up in different gametes during meiosis. The linkage distance of 1cM represents about one million intervening base pairs of nucleotides. A 4cM value would, for instance, represent about a 4 million base pair distance, and a correspondingly larger likelihood of the DNA bits separating during meiosis. If a distance were only a few thousand nucleotide base pairs, the DNA bits would be much more likely to move together. ●




*Machines such as the one above have automated the once-tedious process of determining nucleotide sequence based on the results of electrophoresis (right).*




*A linkage map describes the distance between bits of DNA in terms of how likely they are to be passed on together from parent to offspring. This also shows the physical distance between markers using radiation to fragment the chromosome into pieces.*

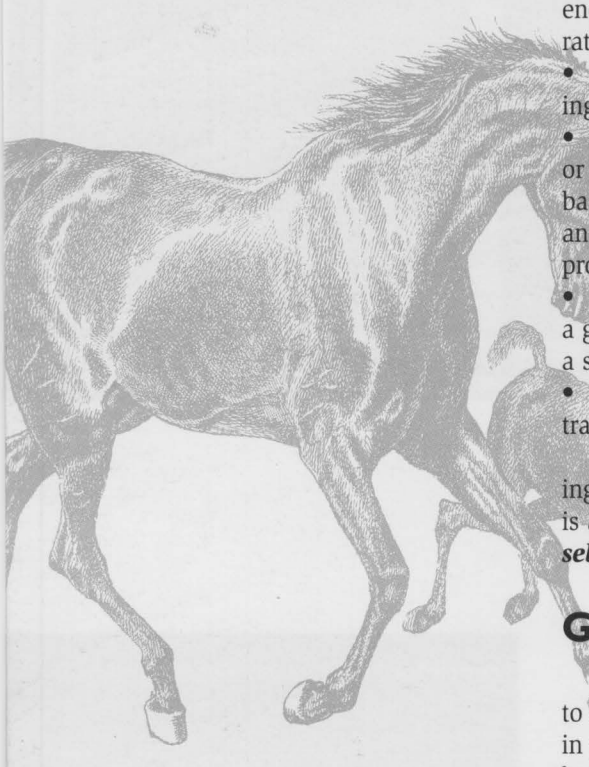
**centiMorgan:** *a measure of how tightly linked two points on a chromosome are.*

**electrophoresis:** *a technique for separating bits of DNA based on how they travel across a gel surface when exposed to an electrical field.*

**linkage map:** *a way of describing genetic material according to the relative location of genes and other bits of DNA.*

# Mapping Applications

*expediting breed improvement*



The "inside look" that genome mapping gives us at the genetic makeup of an animal has tremendous value in livestock breeding. For example, it allows us to:

- determine how inbred a population is, so we can balance the need to maintain breed integrity with the need for a healthy level of genetic diversity, as well as preserve endangered breeds;
- study specific genes to learn how they influence an animal's function and how we might manipulate them to improve production (e.g., genes that influence embryo death in cattle and growth rate in poultry);
- maximize hybrid vigor by maximizing genetic distance in crosses;
- determine parentage to substantiate or disprove claims about the genetic background of specific animals or lines and provide quality control for breeding programs;
- use our knowledge of the location of a gene in one species to find a gene with a similar function in another species;
- locate specific genes for potential transfer to another organism.

But perhaps one of the most promising applications of genome mapping today is a process known as ***marker-assisted selection,*** or ***MAS***.

## Gene Hunting

Say you are a dairy producer trying to increase the concentration of protein in your herd's milk. To do so, you would breed cows with high-protein milk with bulls known to sire daughters that produce high-protein milk. But how would you know which cows and bulls those are? With conventional selection, you would have to rely on milk-protein records gathered through several generations of trial-and-error breeding.

Genetic mapping offers a far more efficient approach. With a genome map, researchers can identify a gene or genes associated with a high milk protein content, or more likely, identify ***markers***—stretches of DNA that flank that gene, that are ***polymorphic*** (come in several varieties), and whose forms are readily distinguished using biochemical tests. Using only a drop of blood, they can test a cow or bull to find out whether the animal has markers known to flank the high-milk-protein gene. If it does, odds are good it has the desirable gene, too.

MAS is valuable for a variety of applications. It can be used to determine disease resistance in healthy animals without having to expose them to disease. It also is helpful in determining whether a young animal will have particular desirable or undesirable characteristics at some later stage (e.g., large litter size or good meat quality) so the producer knows whether to keep or cull it.

The payoff is clear. Marker-assisted selection dramatically improves the speed and accuracy with which we can tailor animals to meet market demands, and reduces the waste and frustration of raising animals like little mystery packages, not really knowing whether they have what it takes to be the best possible carrier of genetic material to their next generation.

## State of the Art

Genetic maps are currently under construction for a variety of livestock and companion animals, including pigs, cattle, chickens, sheep, fish, horses, and dogs. Some mapping efforts have already found commercial application. MAS is now used to select for high milk

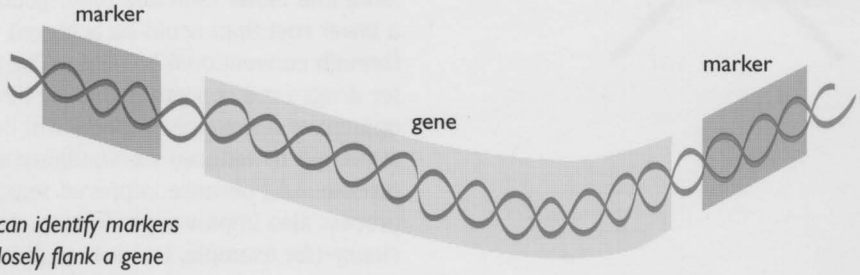
## On the Mark

Exactly what are markers, those mystery bits of DNA that allow researchers to identify the presence or absence of specific genes of interest?

Markers used for marker-assisted selection come in two main kinds. The first, ***Type I,*** is a DNA segment encoding for a protein that, when treated with a chemical scissors known as a ***restriction enzyme,*** splits into chunks (restriction fragment length polymorphisms, or ***RFLPs***) that vary in length depending on which form of the marker is present. RFLPs are currently being used as markers for determining the presence of genes for conditions such as porcine stress syndrome, spider lamb syndrome, and lethal white in horses.

The second kind of marker, the ***Type II*** marker, is based on stretches of otherwise meaningless DNA known as ***microsatellites.*** A microsatellite is essentially a DNA "stutter"—a simple pattern of nucleotides that is repeated over and over. The length of the stutter is polymorphic and is passed from parent to offspring. As a simplified example, in one animal a microsatellite might have 20 "GTT"s in a row while in another it might have 60 "GTT"s. The two versions can be distinguished from each other by the relative distance they travel when separated out from other DNA fragments using electrophoresis.

*Did this bull calf inherit his mother's gene for high milk production? Without marker-assisted selection, the only way to tell would be to wait several years to see if a large number of his daughters are good milk producers.*




*If we can identify markers that closely flank a gene of interest, we can tell with a high degree of certainty whether an animal has inherited that gene by checking for the presence of both markers.*

**marker:** *a section of DNA that is polymorphic (present in different versions) and can be used to identify the presence or absence of a nearby (linked) gene.*

**marker-assisted selection (MAS):** *the use of easily identified bits of DNA to determine the presence or absence of a particular gene and associated phenotype in a particular genome.*

**microsatellite (Type II marker):** *a type of marker made up of a simple pattern of nucleotides repeated over and over.*

**polymorphic:** *a gene or other stretch of DNA that has more than one form.*

**restriction enzyme:** *a protein that cuts DNA at a specific base pair sequence.*

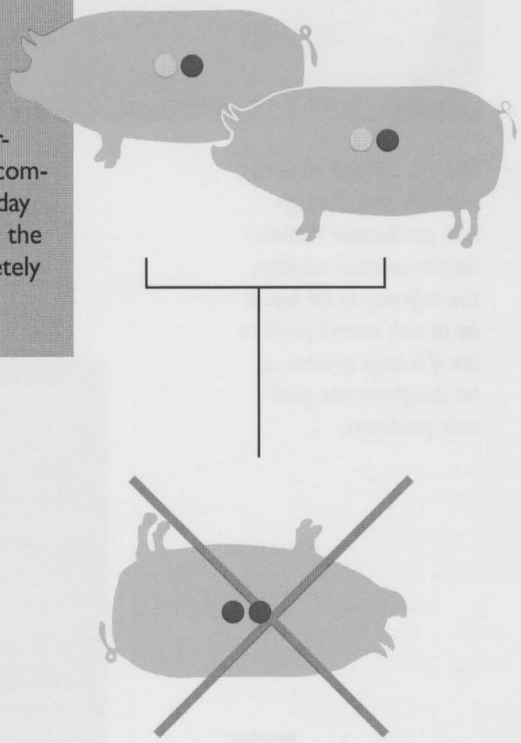
**restriction fragment length polymorphism, RFLP (Type I marker):** *a DNA segment that is polymorphic for length due to the action of a restriction enzyme.*

## PSS Payoff

Among the earliest applications of genetic maps to selective breeding was work in the late 1980s to reduce the incidence of a genetic disease in swine called porcine stress syndrome (PSS). Animals with the gene that causes the disease tend to have more leaner meat than those that do not. If they have two copies of the gene, they also tend to produce mushy, watery meat, and to die when exposed to stress.

Before gene mapping, producers could identify animals with two copies of the deleterious gene by the way they reacted when exposed to a gaseous anesthetic called halothane (pigs were referred to as $Hal^+$ or $Hal^-$). But this test alone could not eliminate the gene from herds because it could not detect animal carriers that had just one copy of the gene.

In the early 1990s, a marker-based test for the gene became commercially available. As a result, today hog producers can readily obtain the information they need to completely eliminate PSS from their herds.

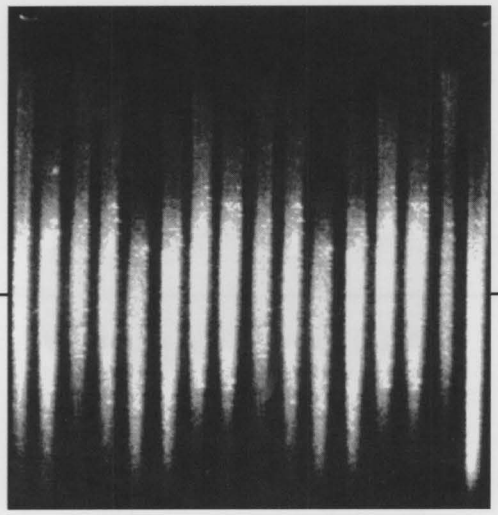


*Hogs with only one porcine stress syndrome allele appear normal, so it's impossible to strategically eliminate them from a population based on phenotype alone. The cost of the disease comes in the next generation: Offspring that inherit both PSS alleles drop dead when exposed to stress.*

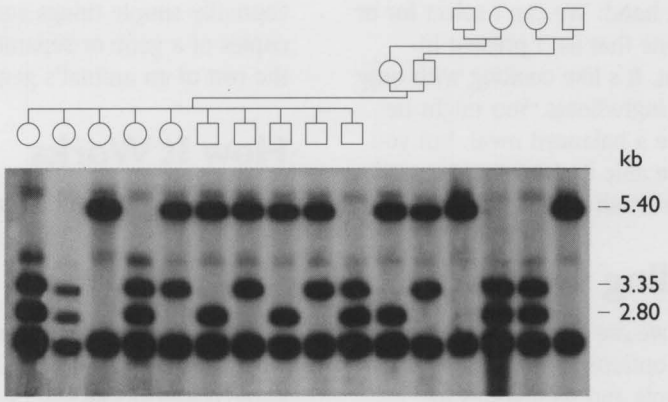
production, superior growth and carcass quality, and increased litter size. It is also helping to improve resistance to various diseases of poultry, cattle, and sheep, and to reduce reproductive failure in swine. In cattle, genetic analysis is being used to cull carriers of genetic disease and to verify the lineage of pedigreed animals. In sheep, producers use mapping to identify carriers of spider lamb syndrome. In horses, mapping has produced tests for the presence of alleles that cause lethal white syndrome in the paint horse breed and for alleles that produce particularly desirable coat coloration.

These few examples are but a fraction of the possibilities. Every day researchers around the world are mapping more and more genes of economic importance and finding new markers. They are even working to apply MAS to traits that result from the interaction of a number of genes, and so involve more complex inheritance patterns than single-gene traits.

As the use of genetic mapping in agricultural animals advances, producers and consumers alike will benefit. Desirable traits can be selected for more quickly and detrimental traits more quickly weeded from a breed's collective gene pool. Producers will be able to offer more and better food and other goods at a lower cost than could be achieved through conventional breeding. The need for drugs (and concern about the development of resistance to them) will be alleviated by reduced susceptibility to disease. And because improved selection process also improves production efficiency (for example, less loss to disease, better conversion of feed to meat or milk), society in general will benefit from a more efficient use of land, feed, and water. ●



*When spotted onto gel and exposed to an electric field, bits of DNA separate from each other according to size.*

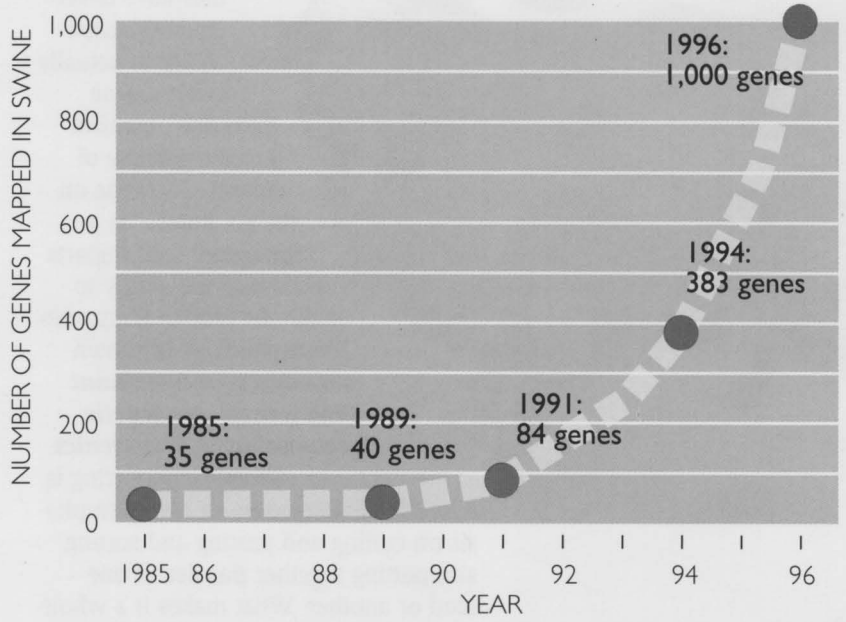



## Stains and Stripes

To determine which version of a genetic marker an animal has inherited, researchers use a sorting technique called ***electrophoresis.***

Electrophoresis works because bits of DNA of different lengths migrate different distances when exposed to an electrical field—much as people with similar interests tend to form clusters of conversation about football, flowers, fractals, Fiats, and so on. To determine which version of a particular marker an animal has, a drop of a solution containing fragments of its DNA is placed on a thin layer of gel. An electrical field is then applied, and various DNA bits begin to migrate across the gel's surface at various rates.

A biochemical process transforms the original sample into an array of stripes. By comparing the striping pattern of an animal with those of its parents, researchers can easily determine which version of a marker allele—and so, which of the associated genes of economic interest—that animal has inherited.




*The number of genes mapped has been growing exponentially in swine and other animals in recent years.*

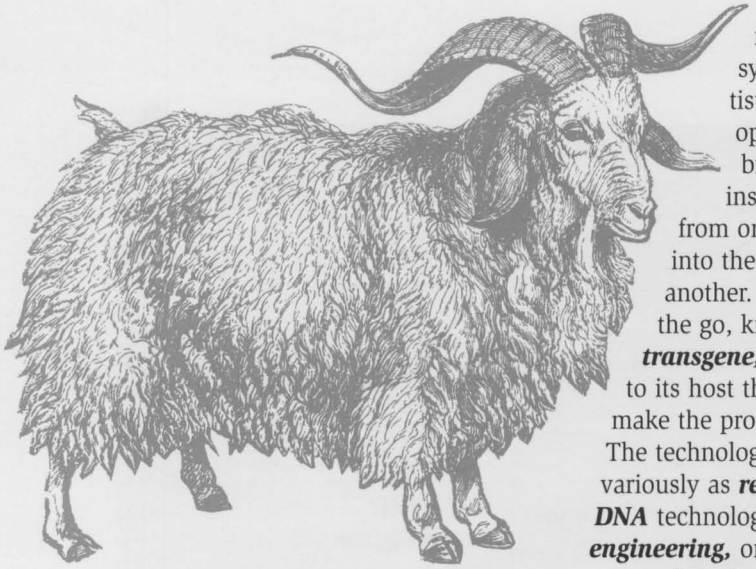
# Genetic Engineering

*genes on the move*

Marker-assisted selection improves animal agriculture by helping us encourage the propagation of alleles that produce desirable traits and discourage alleles that produce undesirable traits. Advantageous as this type of genetic improvement is, it also is limited to what's at hand: We can't select for or against a gene that isn't present in either parent. It's like cooking with only a few basic ingredients. You might be able to make a balanced meal, but you might not be able to cater to dear, rich Aunt Edna's fetish for exotic cuisine.

## Expanding Options

Today we are beginning to expand our genetic options. With a growing supply of tools and techniques for manipulating genes and animals' reproductive systems, scientists have developed the capability to actually insert a gene from one organism into the genome of another. The gene on the go, known as a ***transgene,*** then imparts to its host the ability to make the protein it encodes. The technology is known variously as ***recombinant DNA*** technology, ***genetic engineering,*** or ***transgenics***.



Genetic engineering is a lot like kindergarten—a heavy emphasis on cutting and pasting and sorting and putting together puzzles of one kind or another. What makes it a whole lot more challenging than kindergarten is that we're trying to do all these things with objects so small that they make the period at the end of this sentence look like a football stadium, and that have quite specific constraints on what they will do and when they will do it. As a result, much of the science of genetic engineering has been involved with overcoming logistical obstacles to conceptually simple things such as making copies of a gene or separating it from the rest of an animal's genetic material.

## How It Works

To illustrate how genetic engineering works, let's say you have just discovered a mountainous island inhabited by wild goats that instead of giving milk produce the best cappuccino you have ever tasted in your life. Sensing a grand opportunity, you decide to introduce this capability into domestic goats, which have other desirable production traits—such as large milk volume and a good attitude—not found in the cappuccino goats.

One way to do this, of course, would be to breed wild goats and domestic ones with each other and follow them through successive generations, sorting and resorting the desirable and undesirable traits until you end up with a cross that meets your needs. If you choose this option, you may need to spend decades raising and tending and crossing animals that aren't what you need in order to eventually arrive at the one you do—hoping all the while that demand for cappuccino hasn't disappeared in the meantime.

Genetic engineering, however, gives you another, more efficient option. It allows you to instill the desirable trait into domestic animals without having to wait generation upon generation for genes of the domestic and cappuccino goats to sort themselves out into the combination you have in mind.

To engineer the goat of your dreams, you first physically locate the gene or genes you desire and clone their DNA segment. This is done by isolating DNA from a wild cappuccino goat and breaking it into small pieces using restriction enzymes, a class of proteins that snip DNA at specific nucleotide sequences. Next, you separate the various fragments from each other using electrophoresis, a technique for segregating molecules based on their size.

How can you tell which piece of DNA contains the gene you want? It's not too hard if you know what the cappuccino-making protein looks like. Using special "decoding" molecules, you can use that protein to make a bit of DNA that matches the DNA that coded for it originally, with a fluorescent or radioactive molecule attached to the DNA. This labeled probe is added to your separated DNA. The probe will cling to, and so label, the DNA that contains the gene of interest.

The next step is to add a ***promoter*** sequence. This is a bit of DNA that tells the gene when to switch on and off. All genes have one naturally. In genetic engineering, you can substitute a promoter that lets you choose under which conditions the gene acts—for example, when a certain nutrient is present.

The next job is to get the gene to become part of the genetic material of a cell from the host animal that can grow into a new organism. One method is to use ***pronuclear injection,*** in which a tiny needle inserts hundreds of copies into the about-to-merge nuclei of sperm and egg. This method is very chancy; only a fraction of a percent of cells treated in this way are likely to end up actually expressing the gene.

A more efficient method for adding a gene to an animal, known as ***homologous recombination,*** increases the odds of success by replacing a gene on a chromosome with a more desirable homologous gene in cell culture. Stem cells—undifferentiated cells from an embryo—are allowed to grow and multiply, then exposed to the gene along with an electric shock to make them permeable. Cells that are found to have taken up the gene are used to replace the nucleus of a newly fertilized egg. When implanted into a surrogate mother, with luck this egg will develop into an animal expressing the gene of choice.

Finally, you implant the genetically modified cell into a surrogate mother. If all goes well, the altered embryo will continue its development and become a cappuchino-producing goat.

Each of these steps, of course, involves elaborate, technically challenging manipulations of minute molecules and plenty of "if at first you don't succeed, try, try again." As a result, it takes some time for applications of genetic engineering to move from theory to application. But day by day the techniques and technologies are being refined, added to, automated, and otherwise improved. Within the next few years, the movement of genes, now still a bit of a novelty, may well become a routine part of breed improvement programs. ●

**genetic engineering (transgenics):** *the process of altering the genetic makeup of an animal or plant cell or bacterial plasmid by molecular genetic techniques.*

**homologous recombination:** *the process of replacing a gene on a chromosome with a homologous gene.*

**promoter:** *a piece of DNA that under certain conditions promotes the expression of a gene in specific tissues such as the mammary glands or a muscle.*

**pronuclear injection:** *a genetic engineering technique in which copies of a gene are injected into the host cell with a fine needle.*

**recombinant DNA:** *DNA that contains genetic material from more than one organism.*

**transgene:** *a gene that has been added to an organism's genetic material.*

# Improving Conventional Products

## *genetic engineering and animal agriculture*

*Genetic engineering of stomach bacteria can help cattle and other ruminants use their food more efficiently.*

Though it has only been around for a matter of years, genetic engineering is already changing the world of animal agriculture in many ways. Following are some specific examples of current commercial uses, others that are still under development, and proposals for future application in improving the conventional products we derive from livestock.

## Enriched Feed

Conventional crop improvement already has done much to make corn, hay, and other inputs more suitable as the raw material from which milk, meat, and other animal products are formed. Genetic engineering is taking that improvement one step further by enhancing feeds and forages to better meet food animals' needs for energy, protein, and nutrients. For example, soybeans have been genetically engineered to improve the amount and quality of protein they contribute to poultry and swine feed.

## Better Bacteria

The secret to the exceptional ability of ruminants—cows, sheep, and other cud-chewing animals—to digest vegetation far more efficiently than the rest of us lies in the cellulose-crunching microorganisms that inhabit their stomachs and break down plant cell walls into components they can use. How well the microbes do this affects how well an animal turns its food into products humans can use. Scientists have genetically modified rumen bacteria from cattle so that cows use their food more efficiently, need less costly protein added to their food, and produce better milk.

## Added Inputs

Bacteria and plants are being genetically altered to function as protein factories, mass-producing substances such as growth-promoting hormones that can then be administered to agricultural animals to improve their productivity.

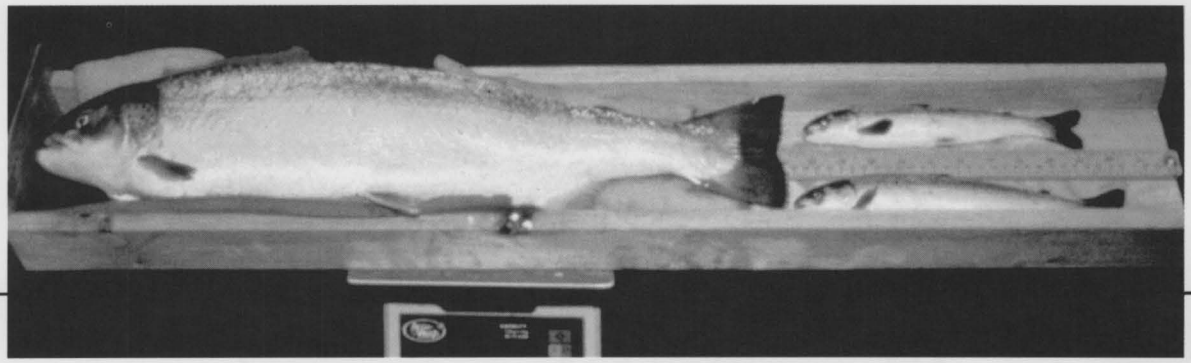
Perhaps the most widely known of such alterations is the genetic manipulation of bacteria to produce a cow hormone known as bovine somatotropin (bST). Scientists have long known that bST can increase milk production in dairy cows, improving the efficiency of converting crops, water, and other inputs into usable products. The problem was finding an economical source of the hormone. Today genetic engineering has produced commercial "bacteria farms" that contain the gene for bST. These crank out large amounts of the hormone, which is then harvested and used by dairy producers to enhance productivity.

## Improved Animal Vaccines

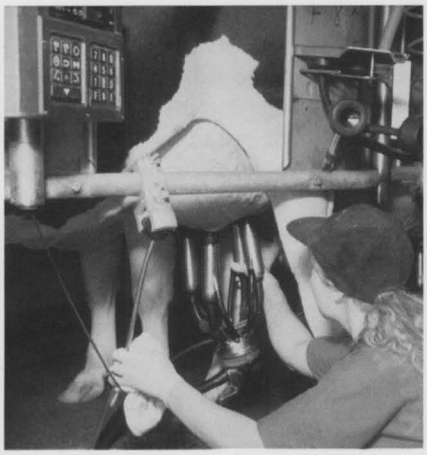
Researchers also use genetic engineering to produce the molecules that generate an immune response to various diseases in animals. These molecules can substitute for conventional vaccines, which use killed or weakened microbes to stimulate an immune response. A genetically engineered vaccine for pig scours is currently available. Other vaccines under development include one against footrot in sheep and another against infectious bursal disease in chickens.

## Increased Individual Productivity

Productivity-related traits of animals (growth rate, litter size, efficiency in converting food to body tissue, fertility, etc.) all have a genetic basis and so can be



*The effects of genetic manipulations can be dramatic. All three of these fish are 14 months old. The genetically altered one (left) weighs 3 kilograms. The unaltered fish (right), at 150 grams each, are normal for their age.*



*Today some dairy cows are given bST, produced artificially by genetically engineered bacteria, to boost their milk production.*

influenced by modifying the animals' genetic makeup. Some of these traits are controlled by multiple genes, so they can't easily be altered by the genetic engineering capabilities we have today. But others can—and have. For example, ***transgenic*** fish have been developed that have their growth magnified by two *thousand* percent.

## Improved Product Characteristics

Animal genomes are also being altered to improve the quality, nutritional value, taste, fat content, and other characteristics of the products they provide. For example, efforts are being carried out to qualitatively alter milk casein content, improving its suitability for cheese-making. Experiments are underway to improve lamb and wool production in sheep. A human gene has been introduced into cows that improves the suitability of their milk for use in infant formulas.

Some animals are even being genetically engineered to produce ***nutraceuticals***—conventional foods that confer some pharmaceutical benefit on those who consume them. For example, cows have been genetically altered so that their milk contains a protein that improves digestion in persons with cancer, AIDS, or other impairments that lead to digestive disorders.

## Improved Disease Resistance

Farm animals are also being improved by adding genes that enhance their natural disease resistance. Researchers are working on inserting a gene into sheep to help them resist scrapie, a fatal disease similar to mad cow disease. This can help reduce the cost of production by reducing the need for antibiotics and vaccines. ●

## Vectors and Zappers

Some genetic engineering involves inserting genes into bacteria rather than into the cells of other animals. To accomplish this, scientists use a ***vector***—a virus, or circular bits of bacterial DNA known as ***plasmids,*** which replicate rapidly to produce engineered genes encoding for economically important proteins. ***Electroporation,*** a process that involves zapping the bacteria with electricity, temporarily disables the fences that keep things from randomly passing through their outside membranes and allows the plasmids to enter the bacterial cell.

**electroporation:** *treatment of a cell with electricity to make it permeable.*

**nutraceutical:** *a food that confers a pharmaceutical benefit when consumed.*

**plasmid:** *a circle of DNA that can be used to carry and make copies of bits of DNA of interest.*

**transgenic:** *containing a gene that was transferred from another organism (same or different species).*

**vector:** *a virus or circular bit of bacterial DNA known as a plasmid that replicates rapidly and is used to transport engineered DNA into cells.*

# Medicines and More

*engineering for nontraditional products*

## Milk Magic

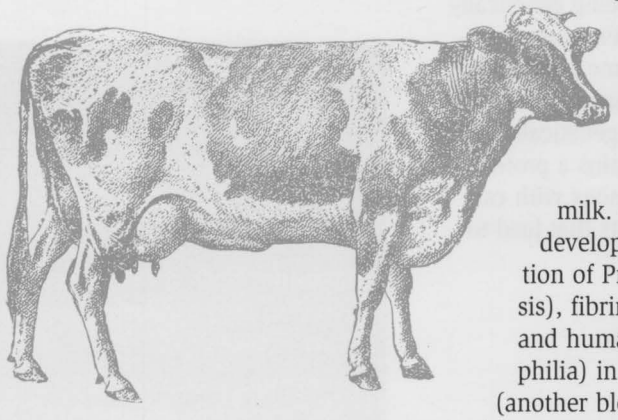
Getting a gene for a human protein into an animal is one thing. But what about getting the protein out? Scientists have ingeniously solved that problem by inserting not only the gene for the desired protein, but also a promoter that limits the expression of the target gene to mammary tissue. The result: The protein is secreted in something the animal already secretes naturally—milk.

In addition to improving our ability to derive conventional goods from livestock, genetic engineering also opens the door to tapping agricultural animals as a source of medicines and even organs and tissues for transplantation.

## People Proteins

A number of human health problems can be treated with proteins normally produced by the body. The problem is, it's exceedingly difficult to produce proteins in the laboratory. As a result, historically such proteins have been obtained by extracting them from donated human blood. This not only is expensive, but also brings fears of infection with HIV and hepatitis.

Today, however, many of these same proteins are being produced, at least on an experimental level, by ***"pharming"***—genetically engineering sheep, cattle, pigs, or other large domesticated lactating animals so they produce proteins for pharmaceutical use in their milk. Clinical trials are now underway for alpha-1-antitrypsin (AAT, a drug used to fight cystic fibrosis) produced in sheep's milk. Other applications under development include the production of Protein C (to treat thrombosis), fibrinogen (a tissue sealant), and human factor IX (to treat hemophilia) in sheep; antithrombin III (another blood clotting aid) and BR96 (a component of an experimental cancer therapy drug) in goats; and human hemoglobin in pigs.



## Xenotransplantation

Genetic engineering is also being used to increase the suitability of organs and tissues from animals—primarily pigs—as replacements for failed body parts in humans.

Ordinarily, moving an organ from one animal into another of a different species, known as ***xenotransplantation,*** produces a massive immune reaction as the recipient fights the "invader" much as it would invading viruses or bacteria. By inserting human genes into a pig, researchers have produced swine whose tissues are treated more civilly by their new host because they are covered with proteins that signal the human body not to go into "search and destroy" mode. Although the organ or tissue may still be eventually rejected, the genetic engineering definitely impedes the immune reaction.

Potential applications for xenotransplantation include not only whole organs, but also islet cells from the pig pancreas to cure diabetes, and the use of porcine liver cells outside the body (in a process much like kidney dialysis) to cleanse blood in persons with liver failure. Researchers hope to eventually overcome the immune reaction completely, making it possible to live a lifetime with an organ from a nonhuman species and so overcoming the limitations created by the scarcity of human organs available for transplant. ●

## What Dolly Did

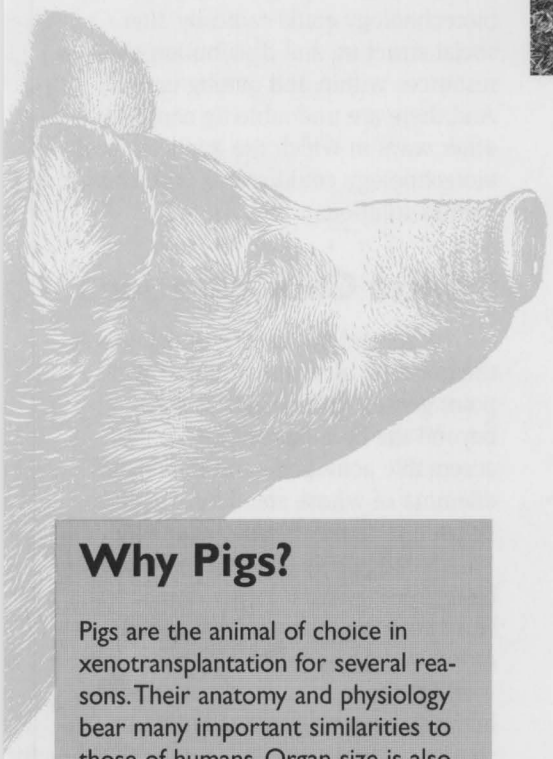
In 1996, in the history-studded countryside of eastern Scotland, a lamb was born that rocked the world. Christened "Dolly," she was the product of the first-ever successful cloning of adult DNA.

Cloning itself is nothing new. Some animals—flatworms, for instance—have been doing it naturally for millennia. And since the 1970s researchers have cloned mammals by disrupting the tiny balls of cells that comprise newly formed embryos, causing them to fall apart into individual cells that each eventually develops into a separate organism. The distinction here is that Dolly was not a copy of another, same-aged creature, but a new generation identical to the previous. Dolly proved that it is possible to clone not just cells of embryos with as-yet unknown traits, but an adult organism that has already differentiated into body parts and functions, clearly expressing the products of its genes. That means being able to know ahead of time what an embryo will be like as an adult.

This achievement was long in coming because in adult cells, DNA is already thoroughly committed to a specific function—producing skin, brain cells, and so on. Like most things adult, in its natural state grown-up DNA just isn't as flexible as the youthful DNA—at least not flexible enough to go back to square one and start a whole new organism.

The Scottish researchers overcame this by treating adult cells with chemicals to remove certain bits of molecules that attach to DNA in the process of specialization. After reinstilling the DNA's flexibility in this way, tried-and-true ***nuclear transfer*** methods got it growing anew. Although the number of failures far outweighed the success—out of 277 fertilized eggs created in this way, Dolly was the only to survive—the researchers did prove it possible to create a genetically identical copy of an adult animal.

Why was that good news? That ties into the researchers' larger goal of developing efficient and cost-effective methods for making pharmaceutical proteins using farm animals. If a normal adult nucleus can successfully substitute for the original nucleus, so might an adult nucleus with a human gene in it. Once a transgenic animal is developed and proves successful at making proteins, researchers could use it to produce other protein producers, rather than starting from scratch each time.



## Why Pigs?

Pigs are the animal of choice in xenotransplantation for several reasons. Their anatomy and physiology bear many important similarities to those of humans. Organ size is also similar, so there are fewer challenges in terms of making things fit than there might be for other species. Third, relatively few diseases are transmitted between pigs and humans. And the fact that many of us already down pork chops and sausage on a regular basis makes the notion of depriving a pig of vital organs for human good more tolerable than doing the same thing for other potential candidates such as nonhuman primates.

**nuclear transfer:** *moving a nucleus from one cell to another.*

**pharming:** *the production of pharmaceuticals using transgenic livestock.*

**xenotransplantation:** *the transplantation of an organ or tissue from one species into another.*

# Beyond Biology

## *social and ethical issues*


*One way to deal with some of the concerns about the risks of biotechnology is to let consumers make informed choices about the products they buy. Some dairy products from milk produced by cows not treated with genetically engineered bST are labeled as such so consumers can choose whether to use them.*

In the last half century, biological science has embarked on an incredible journey. Scientists have discovered how the DNA carries within a space the size of a fraction of a pinprick all the messages a cell needs to become a complete, complex organism. They have developed the ability to modify and move these messages from one organism to another. Thanks to their efforts, we can now improve animals' ability to meet human needs with unprecedented rapidity, breadth, accuracy, and efficiency.

But to what extent is what we can do the same as what we should do? Finding a universally acceptable answer to that question could be the toughest challenge yet in the world of animal biotechnology.

## The Down Sides

One major source of concern in capitalizing on expanding biotechnology capabilities is that when we apply scientific knowledge to practical gain, we almost invariably ended up accruing costs as well as benefits. The internal combustion engine gave us not only a faster way to get around, but car crashes, smog, global warming, and international oil politics as well. Thanks to computer keyboards and cash registers, we have an epidemic of repetitive strain injuries. Is there any reason to expect that animal biotechnology will be different?

In fact, a number of potential "down sides" have already been identified. Some applications could create human health risks by allowing diseases to jump from animals into people. Others could inadvertently add potentially harmful substances to our food. Yet others could deplete diversity, robbing us of potential genetic options for meeting future needs. The capital-rich nature of biotechnology could radically alter social structure and distribution of resources within and among nations. And there are undoubtedly countless other ways in which the application of biotechnology could create problems as well as solutions.

## Ethical Considerations

A second broad area of concern is the question of whether and at what point genetic manipulation strays beyond the boundaries of ethically acceptable activities—and the related dilemma of whose standards ought to be used to make that determination.

Some people are concerned that biotechnology exploits animals. Humans have long used animals for our own gain, whether by eating them, working the land with them, manipulating them as research subjects, or simply enjoying their companionship or the aesthetic value they add to the landscape. Where do we draw the line between acceptable use and exploitation? How do we balance the welfare of humans with the welfare of other living organisms?

Then there's the whole concept of manipulating what some see as the essence of life. Does genetic engineering inappropriately tread on divine turf? Or is gene manipulation simply an extension of selective breeding, an acceptable—even morally necessary—application of intellectual tools to promote the well-being of humankind?

The application of biotechnology to animal agriculture also raises questions of the just distribution of costs

and benefits. Who reaps the benefits of biotechnology? Who pays the costs and bears the risks? Is it ethically acceptable for one group to benefit at the expense of another?

These questions are serious ones. How we choose to answer them will greatly influence the way in which, and extent to which, emerging biotechnological capabilities are incorporated into agricultural practice in the years ahead.

## The Next Step

Does the fact that there are costs and ethical concerns mean we ought to abandon the application of animal biotechnology to meet human needs?

To answer this, we need to recognize that there are also costs and ethical issues involved in not applying these technologies.

If we choose not to use marker-assisted selection to improve the health of livestock populations, we miss an opportunity to reduce production losses due to disease.

If we choose not to boost milk output by genetic engineering, we will likely need relatively more land and water to meet the needs of a growing population.

If we do not pursue the biomanufacturing of pharmaceuticals or genetic alterations that make organs usable for xenotransplantation, we are making literal life-and-death choices for persons with diseases that might otherwise be treated.

To forgo the application of emerging genetic technologies is to bar the doors to immeasurable opportunities to feed a hungry world, reduce the environmental impact of agriculture, and provide medical remedies for the sick and dying.

But that doesn't mean we ought to plow blindly ahead, either. Rather, we must assess potential costs and identify ways to minimize them while maximizing benefits. We must find and apply ways to judge the ethical acceptability of proposed actions.

The decisions we have to make about the application of biotechnology have tremendous implications no matter what route we take. If anything is clear, it is that to make those decisions well, we must understand what it is that we are deciding about. We hope we have contributed to that important goal. ●

## Good or Bad?

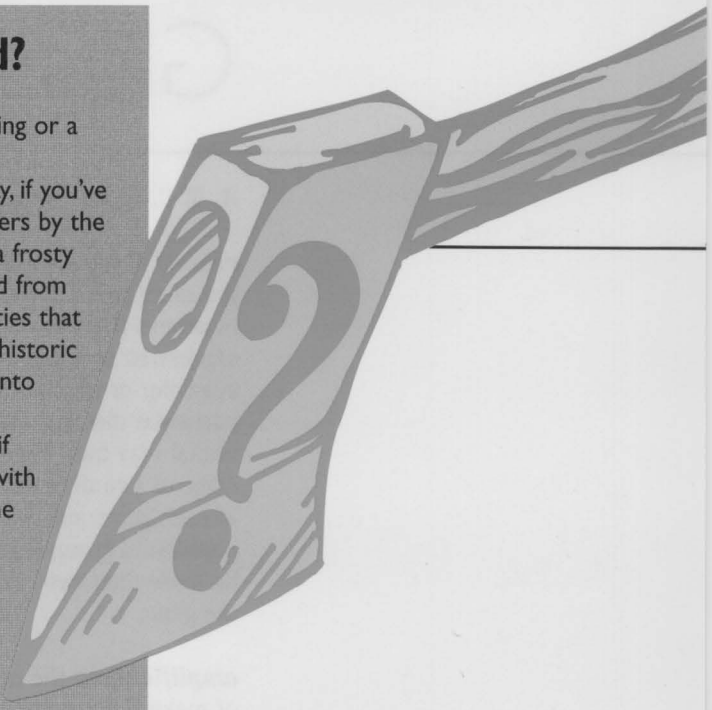
Is an axe a good thing or a bad thing?

Good, you might say, if you've ever warmed frozen fingers by the blaze of a wood fire on a frosty winter night, or benefited from the existence of great cities that have their origins in the historic transformation of trees into towns.

Bad, you might say, if you've gouged your leg with a bad swing, heard tell the tale of Lizzie Borden, or mourned the loss of great pine forests to lumberjacks.

The truth is, an axe is neither good nor bad. It's simply a tool, one that can add to the quality of human life or detract from it, depending on the use to which it is put. Whether it brings gain or loss depends not on the axe, but on how we wield it.

Similarly, biotechnology is a tool. Whether it helps or harms us depends on how we choose to apply it.



# Glossary

***A, T, C, G:*** see *bases.*

***alleles:*** alternative forms of the same gene on two chromosomes that determine the expression of a trait (e.g., eye color or resistance to a particular disease). An individual may have two of the same or two different alleles at each gene, and across a population group there may be more than two alleles at the gene.

***amplification:*** the process of making many copies of a piece of DNA.

***bases:*** the chemical structures along a strand of DNA that form the alphabet of the genetic code. There are four bases, adenine, thymine, cytosine, and guanine. They are often identified by the shorthand labels A, T, C, and G.

***centiMorgan (cM):*** a measure of how tightly linked two points on a chromosome are—that is, how likely they are to be separated during meiosis.

***chromosomes:*** structures found within the nuclei of cells that contain the organism's genetic material.

***cloning (gene):*** the process of isolating DNA to make copies of a gene.

***cloning (organism):*** the process of developing an organism that is genetically identical to another.

***crossing over:*** a process in which homologous chromosomes exchange sections during the process of creating gametes.

***DNA (deoxyribonucleic acid):*** a large polymeric molecule that is made up of nucleotides and other components and that contains the information needed to define structure and function of an organism. DNA is the main nonprotein component of chromosomes.

***economic trait loci (ETL):*** Genes that code for traits that add to or detract economically from the quality, quantity, or efficiency of production of animal goods and services.

***electrophoresis:*** a technique for separating bits of DNA based on how they travel across a gel surface when exposed to an electrical field.

***electroporation:*** treatment of a cell with electricity to make it permeable.

***gametes:*** the cells that carry hereditary material from one generation to the next (sperm and egg).

***gene:*** a stretch of DNA that contains the information needed to create a protein.

***genetic engineering:*** the process of altering the genetic makeup of an animal or plant cell or bacterial plasmid by molecular genetic techniques. Genetic engineering may involve adding a gene, removing a gene, or altering a gene by changing the nucleotides it contains.

***genome:*** all the DNA in a complete set of chromosomes.

***genomics:*** the study of the total molecular material that determines heredity.

***genotype:*** the set of genes found within an organism's cells.

***heterozygous:*** having two different alleles for a particular gene.

***homologous chromosomes:*** the pairs of chromosomes in an animal's genome that carry information for the same types of traits; one of each pair is inherited from its mother and the other from its father.

***homologous recombination:*** the process of replacing a gene on a chromosome with a homologous gene.

***homologues:*** the pairs of chromosomes that carry information for the same types of traits; one of each pair is inherited from the mother and the other from the father.

***homozygous:*** having two identical alleles for a particular gene.

***linkage map:*** a way of describing genetic material according to the relative location of genes and other bits of DNA.

***locus (pl. loci):*** a place (location) on a chromosome.

***marker:*** a section of DNA that is polymorphic (can be present in different versions); the version of a marker carried by an animal can be used to identify the presence or absence of a nearby (linked) gene.

***marker-assisted selection (MAS):*** the use of easily identified bits of DNA to determine the presence or absence of a particular gene and associated phenotype in a particular genome.

***meiosis:*** the process by which sperm and egg (gametes) are formed.

***microinjection:*** a technique used to insert DNA into the pronucleus of a fertilized egg.

***microsatellite:*** a type of marker made up of a simple pattern of nucleotides repeated over and over. The length of the repeat varies between alleles.

***mRNA:*** a molecule that carries information from genes to ribosomes to form proteins.

***nuclear transfer:*** the process of moving a nucleus from one cell to another.

***nucleotide:*** a piece of DNA that includes one of the bases that makes up the genetic code along with the corresponding bit of DNA backbone, made up of phosphate and sugar.

***nutraceutical:*** a food that confers a pharmaceutical benefit when consumed.

***pharming:*** the production of pharmaceuticals using transgenic lactating livestock.

***phenotype:*** the observable characteristics of an organism.

***physical map:*** a way of describing genetic material according to the actual physical structure of DNA (the specific location or sequence).

***plasmid:*** a circle of DNA that can be used to carry and make copies of bits of plant and animal DNA of interest in bacteria.

***PCR (polymerase chain reaction):*** a chemical process used to rapidly make large numbers of copies of DNA segments.

***polymorphic:*** a gene or other stretch of DNA that has more than one form. For example, a gene that codes for eye color is polymorphic, resulting in a variety of eye colors in a population.

***polymorphisms:*** stretches of DNA found in the same relative location on a chromosome but differing in the amount or order of nucleotides.

***probe:*** a piece of DNA that can be used to find a specific sequence of base pairs and is tagged in a way that makes it easy to find (e.g., radioactivity, fluorescence).

***promoter:*** a piece of DNA that under certain conditions promotes the expression of a gene in specific tissues such as the mammary glands or a muscle.

***pronuclear injection:*** a genetic engineering technique in which copies of a gene are injected into the host cell with a fine needle.

***quantitative traits:*** phenotypic characteristics that can be objectively quantified (e.g., milk or egg production). Most quantitative traits are under the combined control of a number of genes physically located on different chromosomes.

***recombinant DNA:*** DNA that contains genetic material from more than one organism and/or that has been mutated to change its level of expression or its characteristics.

***recombination:*** exchange of alleles at two heterozygous loci. This is a result of crossover but does not reflect an even number of crossovers.

***restriction enzyme:*** a protein that cuts DNA at a specific base pair sequence.

***restriction fragments:*** the bits of DNA that result from the cutting action of a restriction enzyme.

***restriction fragment length polymorphism (RFLP):*** a DNA segment that is polymorphic for length due to the action of a restriction enzyme.

***ribosome:*** a structure within a cell that makes proteins.

***sequence:*** to identify the order in which nucleotides appear on a particular stretch of DNA.

***transfection:*** a process used to get DNA into cells. The target cells are placed in a solution containing the DNA.

***transgene:*** a gene that has been added to an organism's genetic material.

***transgenic:*** containing a gene that was transferred from another organism (same or different species).

***Type I marker:*** see *restriction fragment length polymorphism.*

***Type II marker:*** see *microsatellite.*

***vector:*** a virus or circular bit of bacterial DNA known as a plasmid, that replicates rapidly and is used to transport engineered DNA into cells.

***xenotransplantation:*** the transplantation of an organ or tissue from one species into another.

# For Further Information

Biotechnology Industry Organization
http://www.bio.org

Food Animal Biotechnology Center
http://fabctr.umn.edu

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Public Perception Issues in Biotechnology
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FAB

FOOD ANIMAL BIOTECHNOLOGY CENTER

# University of Minnesota FAB Center: Linking Lab and Life

The University of Minnesota Food Animal Biotechnology Center (FAB Center) was established in 1994 as a hub for research, information dissemination, and connection for public and private interests working to apply genetic knowledge to the improvement of animal agriculture. Located in a major land-grant university in the heart of America's leading animal agricultural production region, it connects the University of Minnesota's College of Veterinary Medicine, Medical School, College of Biological Sciences, and College of Agricultural, Food, and Environmental Sciences with public and private sector interests in a unified effort to advance animal biotechnology through basic and applied research, graduate education, and outreach.

In its work to bring together the many players involved in food animal genetic technology, the FAB Center focuses on three main areas of emphasis:

- improving health and disease resistance;
- modulating growth and reproduction; and
- developing genetic maps and markers.

Efforts are underway in each of these areas to advance our basic understanding of biological systems; to train future researchers; and to educate researchers, policy makers, producers, and consumers about current and prospective roles of biotechnology in the advancement of animal agriculture.

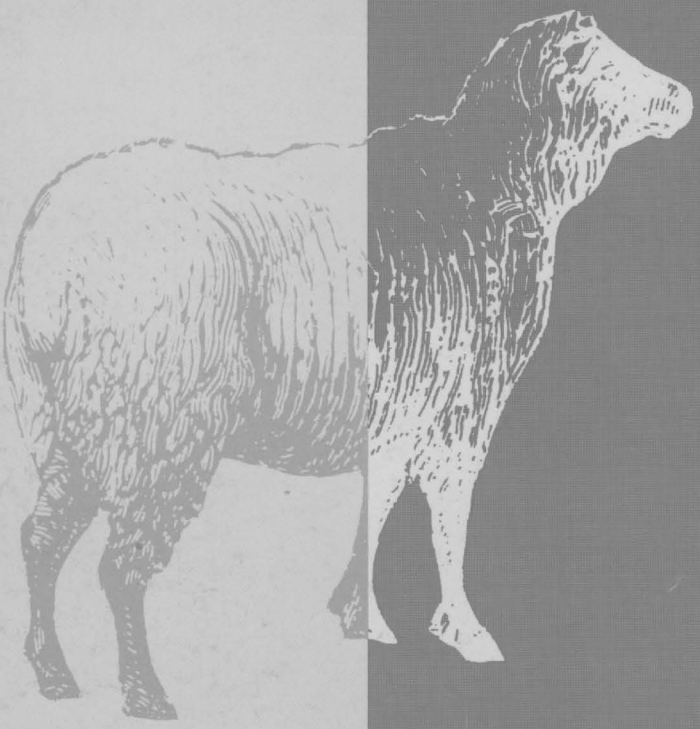
As part of its efforts the FAB Center offers an annual symposium and a variety of continuing education programs. If you would like more information on these programs or on other ways in which the FAB Center is working to apply science to life, please visit our Web site at

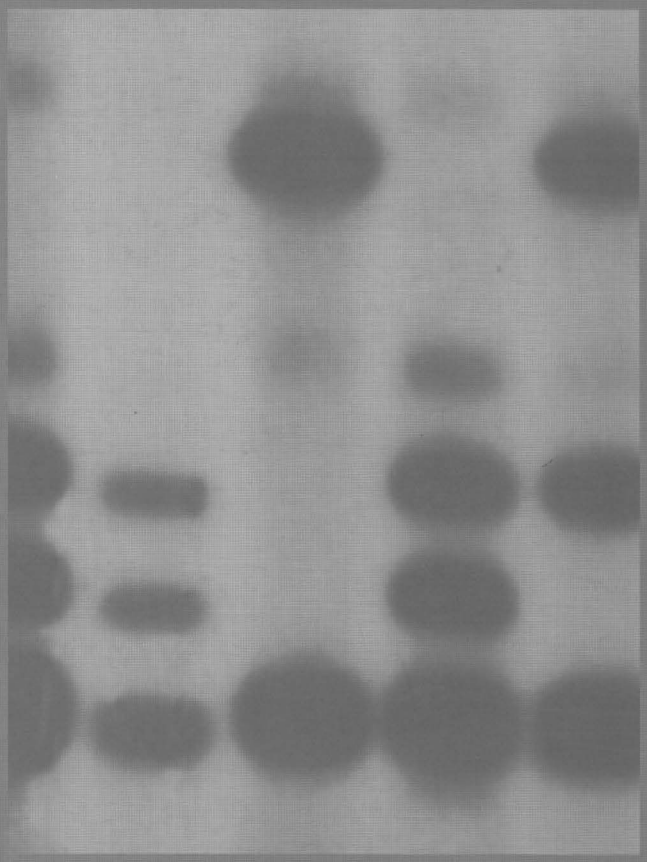
http://fabctr.umn.edu

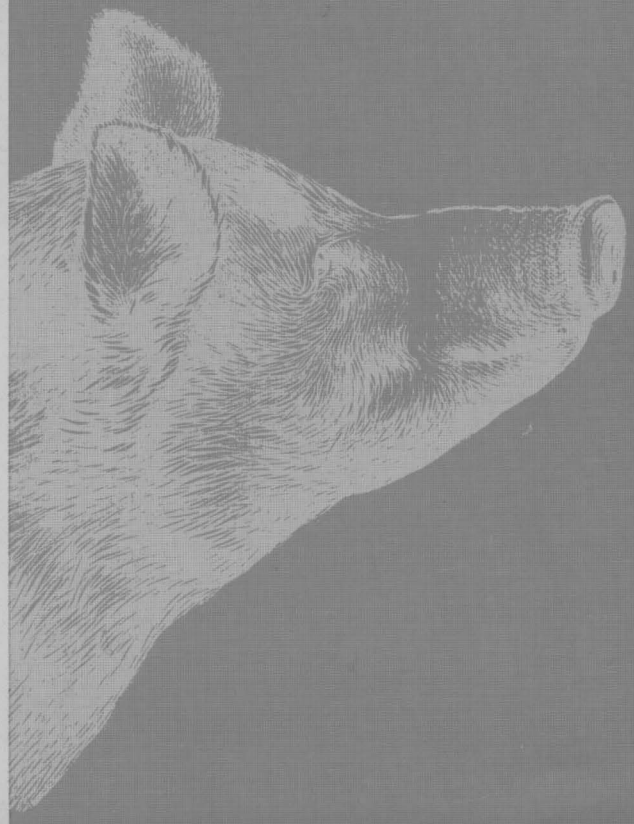
or contact us directly:

phone (612) 624-3025
FAX (612) 624-7284
e-mail fabctr@tc.umn.edu

*FAB Center Mission: To develop competitive, highly integrated food production systems that provide safe, economical food products through the utilization of molecular tools and methods.*







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