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ANIMAL AGRICULTURE'S FUTURE THROUGH BIOTECHNOLOGY, PART I

BIOTECHNOLOGY IN ANIMAL AGRICULTURE: AN OVERVIEW

INTRODUCTION

Since the onset of the modern era of biotechnology, scientists have made impressive strides in developing new agricultural biotechnologies. Biotechnologies that enhance productivity and *productive efficiency*¹ have been developed and approved for commercial use. Technologies that improve productive efficiency will benefit both producers and consumers because feed constitutes a major component (approximately 70%) of farm expenditures. New approaches by which animals may be a source of both biopharmaceuticals for human medicine and organs for transplant (*xenotransplantation*) also are under development.

Advances in biotechnology research have allowed impressive improvements to be made in diagnostic approaches, increasing microbial safety of food and improving animal health. The application of *genomics* and *bioinformatics* in animal agriculture will provide new

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genetic markers for improved selection of all livestock species. Transgenic biology provides a means of altering the genome of animals to achieve desired production or health outcomes of commercial value and societal importance. Biotechnology also offers considerable potential for animal agriculture as a means to decrease the nutrients and odors from manure as well as the volume of manure produced. Development and adoption of these biotechnologies will contribute to a more sustainable environment.

The discovery and development of new animal biotechnologies are part of a continuum leading to the commercialization of agricultural biotechnology products. To enter the marketplace, new products of agricultural biotechnology are evaluated rigorously by the appropriate federal regulatory agencies to ensure efficacy, consumer safety, and

animal health and well-being. To benefit agriculture and society, products of biotechnology must be accepted by consumers. Central to consumer acceptance

¹Italicized terms are defined in the Glossary.

is the need to provide effective population-based education programs to enhance public understanding of the safety and benefits associated with technological advances enabled by agricultural biotechnology. The objective of this paper is to summarize a variety of existing and emerging biotechnologies and their current or potential benefits to societies around the globe. This overview is the first in a series of brief papers introducing several topics related to animal biotechnology.

HUMAN HEALTH: USES OF BIOTECHNOLOGY IN ANIMAL AGRICULTURE TO DECREASE MORBIDITY AND MORTALITY FROM DISEASE

Livestock have long been used to produce medicines for humans. Before the advent in 1982 of recombinant deoxyribonucleic acid (DNA) technology for manufacturing insulin, the insulin needed by diabetics was extracted from animal tissues obtained as a by-product of meat production. Animals also have been the source of products such as heparin (an anti-coagulant), heart valves, various sera and antisera, and collagen (Mohacsi, Thompson, and Quine 1998; Yang et al. 2000).

Advances in recombinant DNA technology, animal embryology, immunology, and other disciplines give rise to the prospect that animals will become important sources of highly sophisticated biopharmaceuticals and biological products.² A number of biopharmaceutical products are being developed in which the ultimate production system will be a genetically modified (GM) animal. In these instances, the gene for the desired molecule is designed and constructed so it can be expressed only in a specific tissue. Several companies focusing on these activities are targeting the production of specific animal proteins in milk (cattle, sheep, goats, pigs) and in eggs (poultry). These new approaches will allow for more economical production of certain pharmaceuticals that currently are expensive to produce. Biotechnological production methods thus may allow for more widespread distribution and application of pharmaceuticals worldwide.

Another type of biotechnology in development involves using animals to produce donor organs for

human transplant. (There is a great shortage of transplant organs from human donors.) Heart valves from pigs have been used for many years to replace heart valves in humans, and several private-sector companies and numerous university scientists are investigating ways to use biotechnology to develop pigs as a source of transplant organs. One key advantage of this approach is the possibility that genetic engineering can be used to produce immune, rejection-free organs. In each instance just described, a vital basic health need will be fulfilled by the use of animals, and no foreseeable alternatives exist.

FOOD PRODUCTION: USES OF BIOTECHNOLOGY IN ANIMAL PRODUCTION

Feeding Livestock

Biotechnology has led to the development of plant varieties with improved qualities including enhanced tolerance of herbicides and protection against viruses and insect pests. These varieties have been adopted rapidly by American farmers, and the United States accounts for approximately 30% of the global area of transgenic crops (James 2001). Genetically modified crops used for livestock feed include corn, soybean, canola, and cotton (cottonseed). In the United States approximately 80% of the corn and 70% of the soybeans are used for livestock feed.

Health and safety are priorities in the development of new food and feed products, including those developed through biotechnological, or “biotech,” means. Evaluation by governmental regulatory agencies is required for each new biotech plant used for feed or food. Scientific studies evaluating feed components derived from GM plants have focused on beef cattle, swine, sheep, fish, lactating dairy cows, and broiler and layer chickens, and have included nutrient composition assessments, digestibility determinations, and animal performance measurements (Alewynse 2000; Beever and Kemp 2000; Faust 2002). Evaluation of nutritional composition has included micronutrients as well as macronutrients such as the content of specific amino acids and fatty acids. Likewise, digestibilities of nutrients derived from GM plants have been compared with feed components from *near-isogenic* control plants and nongenetically enhanced feed sources. Finally, feedstuffs derived from GM plants have been evaluated in performance studies conducted during growth phase and lactation.

Performance results provide very sensitive indications of animal well-being and capture metabolic

²Xenotransplant organs may be classified as biological products under section 351 of the Public Health Service Act (42USC 262) and the Federal Food, Drug and Cosmetic Act (21USC et seq.).

aspects in the use of absorbed nutrients as well as effects on the maintenance of normal physiologic functions. Evaluations have shown uniformly that feed components derived from GM plants commercialized thus far are substantively equivalent in terms of nutrient composition and are similar in terms of nutrient digestibility and feeding value. Overall, feed components of GM plants result in growth rates and milk yields not different from those derived from nongenetically enhanced feed sources (Clark and Ipharraguerre 2001; Faust 2002; Flachowsky and Aulrich 2001). Studies have reported that when corn has been altered genetically for protection against the corn borer, under certain growing conditions GM plants can have lower mycotoxin contamination, resulting in safer feed for livestock (Munkvold, Hellmich, and Showers 1999).

In addition to evaluating the direct effects of feed components derived from GM plants on livestock performance and well-being, research has been conducted to assess the indirect effects involving the digestive fate of the DNA and protein introduced in GM crops, the potential transfer of DNA and protein, and their accumulation in food products such as milk, meat, and eggs (Beever and Kemp 2000). All foods and feeds contain a variety of DNA and proteins from many sources, including plants and animal products. Protein and DNA in feeds and foods, whether from GM crops or nongenetically enhanced sources, typically are degraded during normal digestion. All scientific evidence indicates that DNA introduced in transgenic plants and the proteins they encode are degraded during the normal digestive processes, just as DNA and proteins from nontransgenic plants are degraded. There has been no detection of transgenic DNA or proteins in foods derived from animals that consume feed components from GM plants (Beever and Kemp 2000; Clark and Ipharraguerre 2001; Flachowsky and Aulrich 2001).

Metabolic Modifiers

Advances in understanding the regulation of nutrient use in agricultural animals have led to the development of technologies referred to as *metabolic modifiers*. Metabolic modifiers are a group of compounds that modify animal metabolism in specific and directed ways. They have the overall effect of improving productive efficiency (weight gain or milk yield per feed unit), improving carcass composition

(lean:fat ratio) in growing animals, increasing milk yield in lactating animals, and decreasing animal waste per production unit (NRC 1994).

Two classes of compounds have received major focus: somatotropins (STs) and *β-adrenergic agonists*. Somatotropin is a protein produced by the pituitary gland that differs slightly in structure among animal species. Thus, commercial application of STs depends on the use of recombinant DNA technology to produce the ST protein specific for a species. *β-adrenergic agonists* represent a class of compounds called *phenethanolamines*, and individual compounds differ in their biological effect. The several that affect animal growth are often referred to as *repartitioning agents*. Metabolic modifiers are considered to be new animal drugs and are regulated as such by the Food and Drug Administration's (FDA) Center for Veterinary Medicine.

The most commonly discussed ST is *bovine somatotropin* (bST), which has been administered to dairy cows to achieve increased milk yield, unprecedented improvements in productive efficiency (milk/feed), and decreased animal waste (Bauman 1999). Specific biological mechanisms for the effects that bST has on nutrient-use efficiency and animal well-being have been identified (Bauman and Vernon 1993; NRC 1994). Commercial sales of bST began in 1994, and use gradually has increased so that approximately half of U.S. dairy herds (> 3 million cows) are receiving bST supplements (Bauman 1999). This usage involves herds of all sizes representing a full range of management systems from all U.S. geographic regions. Commercial experiences have demonstrated further that bST supplements result in marked improvements in productive efficiency while maintaining normal cow health and herd life (Bauman 1999; Etherton and Bauman 1998). Bovine somatotropin is being used commercially in 19 countries.

Experimental studies of ST use in growing animals have focused on *porcine somatotropin* (pST). Administration of pST to growing pigs results in greater nutrient use for lean tissue and less for body fat. This shift in nutrient partitioning results in substantially improved feed use, and the shift in lean:fat ratio represents an unprecedented improvement in carcass quality. Biological mechanisms that account for the effects of pST have been delineated and involve coordinated changes in lipid, protein, and carbohydrate metabolism (Etherton and Bauman 1998; NRC 1994). Improvements in dietary protein use ef-

efficiency with pST are especially significant and represent a decrease in the nutrient requirement per unit of lean tissue gain. Porcine somatotropin is undergoing testing required for FDA approval. Worldwide, pST is approved for commercial use in 14 countries.

Supplements of β -adrenergic agonists to growing animals improve feed use and increase the rate of weight gain, carcass leanness, and dressing percentage (NRC 1994). Researchers have established that the mode of action involves changes in endocrine and cellular mechanisms (Moody, Hancock, and Anderson 2000; NRC 1994). The net effect is that these repartitioning agents improve productive efficiency by modifying specific metabolic signals in a coordinated manner to increase nutrient use for lean tissue accretion. Ractopamine is the only β -adrenergic agonist currently approved in the United States—in this instance, for finishing pigs. Its commercial use began in 2000. Worldwide, β -adrenergic agonists are approved for commercial use in 11 countries.

Transgenic Animals

The ability to alter the genome of animals by introducing DNA is a major technological advance in biotechnology and animal agriculture. Transgenic animals are produced by the introduction of a small, isolated, known fragment of DNA into preimplantation embryos. This DNA is inserted into chromosomes of the embryo and is expressed in tissues of the resulting individual. The ability to move genes into organisms also is referred to as *gene transfer* and is a technique of great importance not only to agriculture but to medicine as well.

Production of transgenic livestock provides a method of rapidly introducing “new” genes into poultry, cattle, swine, sheep, goats, and fish without crossbreeding, transporting live animals, or using semen, all of which can be potential means for disease transmission. There are numerous potential applications of transgenic methodology to develop new or altered strains of agriculturally important livestock. Practical applications of transgenic biology in livestock production include improved milk production and composition, increased growth rate, improved feed use and carcass composition, increased disease resistance, enhanced reproductive performance, increased prolificacy, and altered cell and tissue characteristics for biomedical research and manufacturing. Development of transgenic farm animals will allow for more flexibility in the direct genetic manipulation of live-

stock. These modifications are regulated as new animal drugs by the FDA’s Center for Veterinary Medicine.

The overall goals of producing transgenic animals are to enhance the knowledge of biology and biomedicine and to increase the efficiency of milk, meat, and fiber production. To realize these goals, desirable traits must be quantified and the genes responsible for them identified and introduced into production livestock. A process must occur of “select and/or re-design” for populations of superior individuals that can be propagated. It is important to note, however, that the production capability of genetically selected and/or genetically engineered animals will be realized only when their true genetic potential is attained through appropriate environmental and management considerations.

The ultimate utility and value of transgenic technology will be determined by the ability to identify genes for the production of traits desired for improving transgenic animals as well as the ability to incorporate these desired genes, in an appropriately regulated manner, into domestic livestock. The rate at which genetic improvement technologies are incorporated into production schemes will determine the speed at which the goal is achieved of producing livestock more efficiently that meet consumer and market demands.

Microbial Genomics Targeting Food Safety

Advances in biotechnology, microbial genetics, and genomics—especially during the past 5 to 10 years—have greatly affected the development of approaches for assuring the microbial safety of foods, by means of an integrated, farm-to-table framework. Food safety applications of biotechnology and genomics tools have been particularly important in two areas: diagnostic applications, including molecular subtyping methods, and development of animal vaccines for foodborne pathogens.

In 1985, invention and subsequent use of the polymerase chain reaction (PCR) revolutionized biotechnology and many aspects of biology. This method has been applied to develop various foodborne-pathogen detection methods that often are more specific and sometimes more sensitive than traditional culture- or antibody-based detection strategies (Feng 1997). Industry and commercial testing laboratories are using PCR kits and detection systems for specific foodborne pathogens (e.g., *Listeria monocytogenes*, *Salmonella*, or *Escherichia coli* O157:H7). Many PCR assays al-

low rapid, specific testing for foodborne pathogens and thus enable cost-efficient screening for the presence of foodborne bacteria, viruses, and parasites.

In addition to playing an important role in the development of DNA-based detection methods, microbial genomics and biotechnology have had significant impact on improving food safety by providing rapid, discriminatory, and reliable molecular subtyping methods for foodborne pathogens. Application of these methods has facilitated rapid detection of foodborne disease outbreaks and identification of implicated foods; for example, in 1998–1999, a large foodborne disease outbreak occurred due to *L. monocytogenes*-contaminated hot dogs and deli meats (USCDC 1999). In this instance, as well as in other foodborne disease outbreaks occurring in the last few years, molecular subtyping allowed for more rapid outbreak detection and source elimination (thus preventing additional human cases and fatalities) than would have been possible otherwise.

To take further advantage of such molecular subtyping technologies, the Center for Disease Control and Prevention (CDC) and state health departments have established PulseNet, a national molecular subtyping network (Swaminathan et al. 2001). Implementation of PulseNet in combination with widespread adoption of these new technologies likely will have a positive public health impact by helping in the early detection and control of foodborne disease outbreaks.

Application of microbial genomics to vaccine development is covered in the next section of this report, but genetically engineered vaccines for foodborne pathogens have been developed and are available commercially. For example, a genetically engineered *Salmonella typhimurium* double mutant has been shown to prevent colonization of chickens by both *S. typhimurium* and *S. enteritidis* (Hassan and Curtiss 1997). Further advances in the development of GM vaccines will provide an important opportunity to control foodborne pathogens at the farm level.

USES OF BIOTECHNOLOGY FOR ANIMAL HEALTH AND PRODUCTION

Microbial Genomics Targeting Vaccine Development

Infectious animal diseases continue to rank foremost among the most significant factors limiting efficient production in animal agriculture. Furthermore, infectious agents (*zoonotic pathogens*) that are trans-

mitted from animals to humans by way of food and water are an increasing threat to the safety and security of the U.S. food supply and continue to affect human health significantly. Awareness is increasing that animal agriculture likely will lose the use of several important antimicrobial agents and drug classes for two reasons: (1) increased resistance among pathogens and (2) public health threats posed by the potential spread of antimicrobial-resistant zoonotic microbes. Consequently, new approaches are needed to develop improved tools and strategies for prevention and control of infectious diseases in animal agriculture.

Advances in gene discovery in animal pathogens can be expected to identify new proteins and metabolic pathways, thereby providing a foundation for improved understanding of pathogen biology and ultimately aiding in the design of new and effective therapies. Microbial genomics therefore has the potential not only to identify and to characterize new genes (through a functional genomics approach), but also to study the mechanisms governing pathogen development and interactions with their host. Importantly, characterization of genes by means of genomics approaches is a rapid, simple, and cost-effective method of discovering large numbers of new genes and previously unknown biochemical pathways. New disease treatments, whether vaccines or new drugs, must rely on more than empirical methods of discovery and must be based on a fundamental knowledge of pathogen biology and genetics.

The tremendous potential of microbial genomics has led to the development of a focused program of research on pathogens affecting animals and food safety. Notably, of the more than 70 microbes whose genomes have been elucidated completely thus far, two—*Pasteurella multocida* (May et al. 2001) and *E. coli* O157:H7 (Perna et al. 2001)—are of primary importance to animal agriculture. Rapid progress is occurring in sequencing the genomes of many other important food-animal pathogens. An international effort to develop priorities and strategies for animal microbial genomics has been in place since 2000 and has resulted in the development of a list of recommendations for funding agencies and policymakers (USDA 2000). In brief, the U. S. Department of Agriculture (USDA) report has outlined a strategy for identifying the complete sequence of major pathogens of importance to animal health and food safety. The report also highlights the importance of ensuring public access to sequence data to encourage a broad-based

effort by the scientific community to use the information for developing the next generation of tools to detect, treat, and prevent infectious diseases and to facilitate understanding of the infectious disease process.

Although much progress has been made in understanding how microbes are pathogenic, advances in microbial genomics of animal pathogens have not as yet resulted in the development of new diagnostic tests, antimicrobial agents, or vaccines of importance for animal agriculture. In the future this likely will change, particularly in regard to the development of diagnostic tests and vaccines. For instance, genomic sequencing of *Mycobacterium avium* subsp. *paratuberculosis*, the causative agent of Johne's disease in cattle, has led to the identification of several unique genes that will aid in the specific and sensitive diagnosis of infected cattle, thereby enabling development of rational strategies for controlling the spread of and eventually eradicating the disease (Bannantine et al. 2002). Similarly, a large protein that plays a role in the virulence of *Pasteurella multocida* (the causative agent of fowl cholera in avian species, atrophic rhinitis in swine, and hemorrhagic septicemia in cattle) has been identified. This protein is a potential target for vaccine development (May et al. 2001).

Animal Genomics for Production Performance and Disease Resistance

Genomic research provides clues to associations between the incidence and severity of infectious bacterial and viral diseases and particular DNA or protein polymorphisms. These associations provide the impetus for whole-genome searches for such loci in production herds. Before 1993, however, the list of definite susceptibility loci remains relatively short (Guerin et al. 1993). Because no one gene, or no one form of a gene, can confer resistance to all pathogens, even marker-based selection for susceptibility or "resistance" may have to be balanced to ensure that a herd or a population will have an adequate immune response to a variety of pathogens. Alternatively, susceptibility to a specific pathogen, whose presence is confirmed by DNA-based means, could be selected against while maintaining marker and allelic heterozygosity for general immune responsiveness and other production traits.

To identify the genes responsible for genetic variation in host susceptibility to pathogens, genetic

markers that account for a significant portion of genetic variance need to be identified and incorporated into a routine screening procedure. A growing number of quantitative trait loci (QTLs) associated with production have been identified as a result of genetic mapping efforts in livestock. As the human genome effort increases scientific knowledge of the function of genes involved in the complex relationship between host and pathogen, researchers will be able to identify new DNA sequences associated with resistance or susceptibility and to produce genetic markers useful for selection in most, if not all, livestock species.

The use of genetic markers as a DNA-based diagnostic tool for parentage testing (Heyen et al. 1997) also can be applied for other diagnostic purposes—for instance, to DNA fingerprinting of a particular inbred line, a cross, or a herd to provide traceability through the feedlot and packing plant to the consumer (Meghen et al. 1998). Producer and regulator concerns regarding food safety clearly warrant the development of means by which to identify high-quality, biosecure products at the production and retail levels. The potential for livestock producers to use DNA fingerprints to determine herd identity or to track a product from producer to consumer is real and provides the producer with the added value of genetically brand naming or "bar coding" a product as to its uniqueness or origin.

A similar approach can be applied to host susceptibility or resistance to specific pathogens. Scrapie, a member of the transmissible spongiform encephalopathy family that includes bovine spongiform encephalopathy, evidently is transmitted from ewe to lamb at birth or to other ewes exposed to contaminated placental tissues or fluids at lambing. The disease, which leads to deterioration of the animal's brain, is fatal. Infected sheep show symptoms ranging from frequent rubbing against objects to behavioral changes and uncoordinated movements. Scrapie infects sheep that are positive for the susceptible QQ genotype identified by DNA-based means. Sheep carrying at least one R gene are believed to be resistant; those carrying both genes (homozygous RR) seem to be completely resistant (O'Doherty et al. 2000). Use of a PCR-based test on DNA from circulating white blood cells to genotype asymptomatic animals for susceptibility status decreases the need for necropsy to identify the presence of the causative agent in brain tissues in the absence of clinical symptoms.

In addition to providing an opportunity for parentage testing, herd or flock identification, and PCR-based diagnostics of infectious pathogens for herd health purposes, DNA-based diagnostics can be used to identify the presence of genetic mutations that diminish livestock production and animal performance and may even be lethal. Once the mutations altering a protein's function are identified, they can be incorporated into DNA-based tests and used to screen parents to determine whether they are carriers of metabolic or other inherited genetic disorders. This screening is accomplished through PCR amplification of the DNA carrying either the normal or the mutated allele and through determination of whether the DNA sequence can be cut at the site of the mutation by an enzyme specific for the DNA sequence in the normal allele. This technique has been used effectively to identify carriers of inborn errors of metabolism and other phenotypic anomalies in humans as well as in livestock and companion animals.

CONSERVATION OF THE ENVIRONMENT

Impact of Genetically Modified Crops on Animal Manure Management

Meeting the environmental challenges in agriculture is one of the major issues facing the animal industry. Beef and dairy cattle, sheep, swine, and poultry in the United States produce more than 160 million metric tons of manure (dry matter basis) annually (Sweeten 1992). Most swine and poultry waste is produced in confinement units for which the nearby land base often is insufficient to accommodate waste in an environmentally sound manner. Animal manure, especially that of swine and poultry, is high in nitrogen (N) (4.7 to 5.1%) and phosphorus (P) (1.6 to 3.0%), both of which can contribute to surface and groundwater pollution. In addition, ammonia and other nitrogenous and sulfurous gases contribute to poor air quality and offensive odors. Several GM crops have been developed or are being developed to address the environmental issues related to N, P, and total manure excretion and odors.

Genetically Modified Crops That Decrease Phosphorus Excretion

Phosphorus content in swine and poultry manure is high because these species consume diets consisting of cereal grains and oilseed meals in which most (60 to 80%) P is bound organically as phytic acid or

phytate. Because of the lack of phytase in their digestive tract, nonruminants are unable to degrade phytate, and most P from these feed ingredients is excreted in the feces. In addition, relatively large amounts of inorganic P must be fed to pigs and poultry to meet their P requirements; consequently, fecal P excretion is increased further. Ruminants use phytate quite efficiently because of the abundance of phytase produced by rumen microorganisms.

The mutant *lpa1* gene in corn (Raboy, Dickinson, and Neuffer 1990) interferes with synthesis of phytic acid in corn seeds without affecting total P. Low-phytate corn contains half as much phytate P (0.10 vs. 0.20%) and greater than three times as much inorganic P (0.18 vs. 0.05%) as near-isogenic, conventional corn (Cromwell et al. 1998). Recent studies have shown that the bioavailability of P is considerably greater in low-phytate corn than in conventional corn for pigs (77 vs. 22%, respectively) and for chicks (52 vs. 10%, respectively), so less inorganic P is needed in the diet to meet the P requirement when low-phytate corn is used. As a result, 30 to 40% less P is excreted when low-phytate corn is fed to pigs and chicks (Pierce and Cromwell 1999; Spencer, Allee, and Sauber 2000).

Another biotechnology crop, low-phytate, low-oligosaccharide soybean (Hitz et al. 2002), has the potential to decrease further the excretion of P by nonruminants. Soybean meal from low-phytate soybean has less phytate P (0.22 vs. 0.48%) and more inorganic P (0.55 vs. 0.22%) than soybean meal from near-isogenic conventional soybean does, and the P in low-phytate soybean meal is more than twice as bioavailable as that in conventional soybean meal for pigs (49 vs. 19%, respectively) and for chickens (58 vs. 28%, respectively). Thus, less P is excreted (Cromwell et al. 2000a). Diets containing both low-phytate corn and low-phytate soybean meal have resulted in 50 to 60% decreases in P excretion by pigs and chicks (Cromwell et al. 2000b,c).

To date, biotechnology has been used to insert the phytase gene into pigs (Golovan et al. 2001) as well as into alfalfa (Ullah et al. 2002) and canola (McHughen 2000), and the phytase activity in pigs' saliva and in both crops has been increased greatly as a result.

Genetically Modified Crops That Decrease Nitrogen Excretion

Most N in animal manure originates from dietary sources. Most fecal N comes primarily from

dietary protein that is not digested in the digestive tract, and most urinary N arises from absorbed amino acids in excess of animal requirements. Small amounts of excreted N are from the intestinal tract and other endogenous sources.

Biotech crops with improved amino acid profiles have the potential to decrease N excretion significantly, especially in nonruminants. Increased levels of lysine, methionine, tryptophan, threonine, and other essential amino acids in grains would mean that the essential amino acid requirements of pigs and poultry can be met with lower-protein diets containing fewer excesses of other amino acids that eventually must be degraded to urea N and excreted in the urine (Carter et al. 1996). Moreover, feeding of low-protein diets results in less production of ammonia and other volatile gases from manure that diminish air quality and cause objectionable odors (Turner et al. 1996).

Corn containing the mutant *opaque-2* or *floury-2* gene is an example of a cereal grain having a comparatively high level of lysine, tryptophan, and methionine (Mertz, Bates, and Nelson 1964). Other cereals have been, or are being, developed with improved amino acid profiles (Villeagas, Vasal, and Bjarnason 1992) or increased free lysine levels (Anderson 1998).

In the future, transgenic plants will be developed with improved capacities to assimilate N into higher-quality, more-digestible proteins with improved amino acid profiles (Hartnell 2000). These products will improve the overall quality of protein consumed by both ruminants and nonruminants and will decrease N excretion into the environment.

Genetically Modified Crops That Decrease Total Manure Excretion

Development of new biotechnology crops will affect total manure production. For example, high-oil corn was released in the mid-1990s for livestock feeding. Feed intake is decreased when high-energy diets containing high-oil corn are fed and, subsequently, manure output is decreased. Biotech forages with decreased lignin or with more easily degraded cellulose and hemicellulose are on the horizon (Hartnell 2000). Already, the brown midrib mutant gene, which decreases lignin in corn by as much as 40%, has been bred into certain lines of corn. Furthermore, lignase, cellulase, and hemicellulase enzymes may be bioengineered into plants to enhance use of these energy sources, thereby decreasing ma-

nure output (Hartnell 2000). Low-oligosaccharide soybeans also have the potential to decrease manure volume as a result of improved energy digestibility in nonruminants.

In summary, biotechnology offers considerable promise to the animal industry for decreasing nutrients and odors from manure, as well as for decreasing overall manure production. These changes will contribute to a more sustainable environment.

ETHICS IN ANIMAL BIOTECHNOLOGY

Ethical concerns about animal biotechnology usually fall into one or more of four major categories: (1) impacts on human health and safety, (2) animal welfare and animal rights, (3) environmental impacts, and (4) concerns that certain technologies are “unnatural” or amount to “playing God.” Practically and politically, all four categories are important because various interest groups and the public at large are generally concerned about all four, but supporters of animal biotechnologies should address the first two and at least be conversant with issues in the third category. The reason is that the first and second categories are the least problematic, philosophically, insofar as it is relatively easy to articulate a coherent and convincing ethical viewpoint that takes these issues seriously, in sharp contrast to the fourth category. And the third category is either problematic in a similar way or reduces to concern for the first two.

It is difficult to define “unnatural” in a way that both distinguishes the new biotechnologies from traditional agricultural technologies and also makes doing what is unnatural a “bad” thing (Comstock 2000; Rolston 1979). Both expressions have strong rhetorical appeal but are probably best interpreted as shorthand ways of expressing concerns that fall into one or more of the other categories. For instance, when a lobbying group describes a technology as unnatural, the group almost certainly has concerns about risks to humans, animals, and/or the environment, and it is on these concerns that proponents of biotechnology should focus.

Concern for the environment may be either “instrumental” or “intrinsic.” In the first instance, the concern is that what happens to the environment will in turn affect humans or animals deleteriously. In the second instance, the concern is for the environment such that the environment is *itself* thought, in some holistic sense, to be an object of direct moral concern. But in this sense, the moral standing of the environ-

ment can be problematic (Sober 1986; Varner 1998).

Relative to ethics and agricultural biotechnology, the two most important topics for philosophical research are related to (1) the various kinds of risks posed to humans and (2) the question of how to factor animal well-being into policy decisions. Regarding the first topic, controversial applications of biotechnology to plant products already have illustrated that public concerns about food safety are deep seated. Scientists tend to see the application of biotechnology as a purely scientific question, but Comstock (2001) and Thompson (1987) suggest that there are other important conceptual issues in the background.

Regarding the second topic, publicity surrounding cloning may heighten public concern about the ways in which scientists factor animal welfare into research decisions. Although cloning may prove to be of little value in agricultural contexts, related media reports constantly quote researchers as stressing that the cloning of humans would be unacceptable in light of the low success rate and the high rate of health problems in animal clones. This emphasis, by researchers themselves, that cloned animals are likely to have health problems draws increased attention to the questions of how scientists conceive of animal welfare and how they factor adverse welfare impacts on animals into decisions of whether or not various lines of research are justified (Varner 1999).

CONCLUSION

Agriculture is transiting a remarkable scientific era with respect to the myriad of novel processes and products that have been developed using biotechnology. These new biotech processes and products already have provided tangible benefits to agriculture and to society. Moreover, many new products of biotechnology are being developed that will benefit the food sector. Development and adoption of novel biotechnologies will be crucial in meeting the challenge of producing enough food for a growing world population while minimizing and reducing impacts on the environment. The impact these technologies have on society in the future, however, will be largely dependent on the extent to which they are adopted by producers and the agricultural community and accepted by consumers.

Questions about societal impacts and safety often arise as the result of technological change. Inherent in the successful development and adoption of new and emerging biotechnologies for agriculture is the

need to increase public understanding of the associated scientific, economic, legislative, ethical, and social issues. This paper and subsequent papers in this series will, hopefully, help address these issues.

ADDITIONAL TOPICS IN THE SERIES

ANIMAL AGRICULTURE'S FUTURE THROUGH BIOTECHNOLOGY

Future issue papers, which have been approved by the CAST Board of Directors, will follow in this series:

1. Animal Productivity and Genetic Diversity: Transgenic and Cloned Animals, Xenotransplantation, and Stem Cell Research
2. Animal Organ Donors: Current and Potential Applications in Human Health
3. Food and Feed Safety of Biotechnology-derived Crops Fed to Livestock: Safety of Human Consumption of Milk, Meat, and Eggs
4. Metabolic Modifiers for Use in Animal Production
5. Role of Biotechnology-derived Animals in the Development of New Medications for the Treatment of Human Disease
6. Vaccine Development: Recombinant DNA Technology for Animal Health and Food Safety Through Microbial Genomics
7. Environmental Impacts of Biotechnology-derived Crops on Animal Manure Nutrient Management
8. Ethical Perspectives on Animal Biotechnology

GLOSSARY

β -adrenergic agonists. A class of compounds called *phenethanolamines*.

Bioinformatics. The research, development, or application of computational tools and approaches for expanding the use of biological, medical, behavioral, or health data, including those to acquire, store, organize, archive, analyze, or visualize such data—particularly large databases that are difficult to analyze by traditional biostatistical methods.

Bovine somatotropin. A naturally occurring protein produced in the pituitary gland of cattle.

Recombinantly derived bovine somatotropin is approved by the FDA for administration to dairy cows to increase milk yield and improve productive efficiency (milk/feed).

Gene transfer. The ability to transfer genes from one organism into the same or other species.

Genomics. The science that studies how the DNA of any species is organized and expressed.

Metabolic modifiers. Biotechnology products that regulate nutrient use in agricultural animals

Near-isogenic. A change in one or more genes that results in an intended effect, leaving the remainder of the plant like the unchanged version.

Phenethanolamines. A class of compounds all of which contain a phenol, ethanol, and amine group.

Porcine somatotropin. A protein produced by the pituitary gland of pigs that is administered to growing pigs to achieve greater nutrient use for lean tissue and less for body fat. This shift in nutrient partitioning results in substantially improved feed use and an unprecedented improvement in carcass quality.

Productive efficiency. Weight gain or milk yield per unit of feed.

Rep partitioning agents. β -adrenergic agonists and individual compounds affecting animal growth.

Xenotransplantation. The use of animals as a source of tissues for human medicine and of organs for transplant.

Zoonotic pathogens. Infectious agents transmitted from animals to humans.

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