

## HOW BIOTECHNOLOGY IS AFFECTING THE REALITY OF ANIMAL NUTRITION

Kyle Newman, Ph.D.  
Venture Laboratories  
[www.venture-labs.com](http://www.venture-labs.com)

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There are already a number of examples of Biotechnological advances that have positively impacted animal nutrition. The use of the enzymes such as phytase in animal feeds was cost prohibitive with normal gene expression of the phytase enzyme. However, a better understanding of the growth requirements and nutrients for the microbes that produce the enzyme has led to an economical alternative to high supplemental phosphorus diets. Zeranol, the active ingredient in the cattle implant Ralgro™ is manufactured by a fermentation process maximized through biotechnology and delivered through an implant designed to erode at a controlled rate. In addition, modifications to field crops can enhance the nutrient profile available to the animal. The application of biotechnology in agriculture is at its' infancy and the implications for future development are amazing.

In April of 2003 the International Human Genome Sequencing Consortium announced the completion of human genome project. While this may seem unrelated to animal nutrition, it lays the groundwork for changing the way we will produce livestock and treat disease. Already designer drugs are being manufactured based upon the human genome project, this is the science of pharmacogenomics. The science of nutrigenomics looks at the molecular basis for how nutrition can impact health by altering the structure or expression of individual genes. The implications of nutrigenomics have always been present, just not understood. Why, for example, can some people eat fried foods, consume too much alcohol and smoke and live long, prosperous lives, while others under the same diet do not fare as well? An example of a single gene influence on health is phenylketonuria (PKU) which is a recessive trait expressed as a defect in the enzyme phenylalanine hydroxylase leading to an accumulation of phenylalanine in the blood which can cause neurological damage (Kaput and Rodriguez, 2004). For this reason, foods containing aspartame contain a warning cautioning phenylketonurics to avoid consuming this food. As the area of nutrigenomics advances, we will begin to see methods to detect dietary factors that impact animal production at the cellular level, that, in-turn improve animal performance. The end result may be that animal trials will progress beyond “feed ‘em and weigh ‘em” to the progression from one phenotype to another through changes in gene expression

In February of 2003, the magazine Technology Reviews identified “10 Emerging Technologies That Will Change the World.” In this article, Glycomics was one of two bioscience fields identified as having dramatic potential to change the way we live (the other being injectable tissue engineering). Glycomics is defined as the characterization of the sugars and the structure of these sugars that make up a cell. Mention was already made of the quest to

define the human genome (the full DNA complement) that was recently completed. Many are aware of proteomics, which is the study of the full set of proteins encoded by a genome, but very few people are aware of glycomics. Putting these sciences in perspective, genomics was child's play compared to the undertaking of proteomics, which is dwarfed in terms of complexity when compared to glycomics.

At one time, it was thought that there were three main roles of carbohydrates in biological systems; as an energy source, structural component (cellulose, chitin) or as glycoproteins or glycolipids and subsequently needing to be stripped away in order to truly understand the function of the protein or lipid. However, it turns out that the sugars on these proteins can define their function or serve to stabilize the compound. A good example of this stabilization is industrial-grade enzyme production where shelf-life and heat stability have been enhanced by glycosylation of the protein.

It turns out that sugars play a role in many disease processes and glyco-therapy may be part of the answer to antibiotic resistance. Bacterial infection is due in many cases to the ability of bacteria to recognize host cell surface sugars and attach to these sugars. In the case of pathogens, colonization and disease in the animal may follow. One way to prevent pathogens from causing disease is to prevent them from attaching to the epithelial cells in the gut. Early studies using mannose in the drinking water of broiler chicks demonstrated that this therapy could reduce colonization rate of *Salmonella typhimurium*. Purified mannose and a complex sugar called mannan oligosaccharide (MOS) have been successfully used to prevent bacterial attachment to the host animal by providing the bacteria a mannose-rich receptor that serves to occupy the binding sites on the bacteria and prevent colonization in the animal (Oyofe, et al., 1989; Spring, et al., 2000). Mannose specific adhesins (the binding entity on the surface of bacterial cells) are used by many gastrointestinal pathogens as a means of attachment to the gut epithelium.

Several studies have been conducted examining the role of mannans and their derivatives on binding of pathogens to epithelial cells in the GI tract. *E. coli* with mannose-specific lectins did not attach to mammalian cells when mannose was present (Salit and Gotschlich, 1977). Spring and coworkers (2000), used a chick model to demonstrate that MOS could significantly reduce the colonization of *Salmonella* and *E. coli*. Animal trials in other species show similar benefits in reducing pathogen concentrations.

In dogs, as well as trials in poultry, reductions in fecal clostridial concentrations have also been noted with MOS supplementation ( Finucane et al., 1999; Strickling, 1999).

Fructooligosaccharides (FOS) have also been examined for pathogen inhibition. The principle behind the use of FOS involves the structure and bonding of the fructose molecules. Purified preparations of FOS have been shown to provide a nutrient source for beneficial bacteria such as Bifidobacteria and certain lactobacilli. By supporting the growth of the beneficial bacteria it is thought that this will provide an *in situ* competitive exclusion (CE) effect, thus improving animal health. However, it seems important that the concentration of non-complexed fructose molecules be kept to a minimum in order for this oligosaccharide to be successful. Oyarzabal and coworkers (1995) found that *Salmonella* ssp. could not use a purified fructooligosaccharide (FOS) preparation for growth but were able to utilize a commercial preparation of FOS. The authors suggest the use of lactic acid bacteria in combination with FOS as a feasible approach to control *Salmonella*. Other studies have demonstrated a reduction in *Salmonella* concentrations in birds challenged with *S. typhimurium* with and without FOS and a CE culture. FOS alone had

little effect on Salmonella exclusion when FOS was administered after infection but FOS in combination with a defined CE product had an additive effect on Salmonella exclusion especially when used as a prophylactic prior to Salmonella infection (Bailey *et al.*, 1991). Waldroup and coworkers (1993) found that supplementing broilers with 0.375% FOS had few consistent effects on production parameters or carcass Salmonella concentrations. These authors also caution of possible antagonism between FOS and BMD. Human data for FOS is much more consistent. Hidaka *et al.* (1986) found that consumption of 8-g/day FOS increased numbers of bifidobacteria, improved blood lipid profiles and suppressed putrefactive substances in the intestine.

Other investigators have examined glycomics as a tool against bioterrorism. A recent trial in mice found that mice receiving yeast glucans for 1 week prior to anthrax infection had double the survival rate of unsupplemented animals. As a therapeutic agent, mice receiving yeast glucans had a 90% survival rate compared to 30% survival for control animals (Kournikakis *et al.*, 2003).

Glycomics also plays a vital role in viral diseases. Avian influenza represents a huge threat to the poultry industry. Avian influenza binds to  $\alpha$ -2,3 sialic acid-galactosyl linkages, but human influenza binds to the  $\alpha$ -2,6 linkage. This explains the low mortality in humans, however, the pig trachea has receptors for both  $\alpha$ -2,3 and  $\alpha$ -2,6 sialic acid linkages, is susceptible to both human and avian influenza and has been called a mixing pot for avian influenza alterations that allow it to infect humans (Ito *et al.*, 1998). Recent data suggests that ciliated cells also play a role in influenza infection (Matrosovich *et al.*, 2004). Sulfated galactomannans also demonstrate *in vitro* and *in vivo* activity against the flaviviruses, yellow fever virus and dengue virus (Ono *et al.*, 2003). West Nile virus has also gained a strong foothold on the United States affecting birds, horses and man. N-linked sugars with mannose residues on the cell membrane protein were found to be important in West Nile virus binding to the cell (Chu and Ng, 2003).

The use of biotechnology and nutrition is in its' infancy. Nutrigenomics and understanding the genome of livestock species will help define the interactions of nutrition, immunology and disease. While mannan oligosaccharide is currently being used to improve health and production of animals, there are enormous possibilities to use other sugars as possible agents against pathogen infection. To say that carbohydrates are involved in just about every aspect of biological sciences is not an understatement. Finding ways to exploit them is the current challenge. The vast array of possibilities that exist with polysaccharide structure and function make glycomics a science that may well pass on to future generations. We have only scratched the surface but already we have used our limited knowledge to take advantage of the "sweet tooth" of pathogens to control infection.

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