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DNA ASSISTED SELECTION – A REALISTIC PERSPECTIVE

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INTRODUCTION

Breathtaking advances are occurring in the knowledge and understanding of the structure, sequence and function of DNA. The entire genetic blueprint, or DNA code, has now been deciphered for humans, mice and a variety of other organisms. This modern-day "Genomic Revolution" may be one of the most important periods in the scientific history of humankind, promising diagnostics and therapeutics for numerous diseases and maladies.

In animal agriculture, and particularly in beef cattle improvement, the payoffs of the "Genomic Revolution" have seemingly been few and far between. DNA information on cattle is now routinely used for determining parentage and for quality control, and a handful of DNA diagnostic tests are available for a small number of relatively simple traits. However, the true potential of harnessing genomic technologies in beef cattle awaits application of DNA testing for production traits such as carcass composition and quality, growth, reproduction and overall health status. If properly developed and delivered, these diagnostic tools may assist genetic improvement by increasing accuracy of the selection process, while simultaneously lowering the time required in order to reach and effect selection decisions. Alternatively, DNA tests can be used as tools to sort cattle and properly match a genetic profile with management decisions such as feeding and use of implants. In the long-term, assuming public acceptance of GMOs, the cattle genome may eventually be engineered to design novel animals and beef products.

DNA MARKERS I: PARENTAGE AND IDENTIFICATION

The first application of DNA information in beef cattle genetic improvement has been in providing highly accurate forms of identity testing. By evaluating a panel of 10-15 highly variable genetic markers, an extremely unique genetic "fingerprint" of an individual can be obtained. Several uses of this relatively simple technology are apparent. Primary among these is the determination of parentage. In addition to the obvious utility of determining parentage for registration, sale, embryo transfer and associated purposes, DNA-based sire verification enables use of multi-sire breeding schemes. This latter application may contribute to genetic improvement by enabling retrospective selection; for example, high or low quality carcasses may be traced from the kill-floor back to sire of origin, allowing for selection/culling of sires with high/low genetic potential for carcass traits. It is likely that miniaturization of the genotyping process (i.e. gene chips), in combination with robotic automization, will render DNA fingerprinting a simple and relatively inexpensive tool for the beef cattle industry in the future.

The ability to trace the identity of a sample throughout a complex production chain-of-custody is another application of DNA-based identity testing. While not necessarily directly related to genetic improvement, traceability of DNA from meat to carcass to individual animal may become an integral component of quality control and food safety programs in the beef industry. A feasible strategy would be large-scale, inexpensive storage of simple DNA-containing samples (e.g. blood spots, hair), while reserving full DNA analysis only for those samples that are called into question or for random quality control purposes.

DNA MARKERS II: DNA-ASSISTED SELECTION - BACKGROUND

Selection based on phenotypic records has been the driving force behind genetic improvement of beef cattle throughout history. By combining information on an individual's performance with the performances of ancestors, sibs and progeny (i.e. EPDs), breeders are able to statistically predict the animal's genetic potential with relatively high accuracy. Selection has proven to be an extremely powerful tool to change production characteristics within a population.

Along the course of animal breeding history, several new tools have emerged to enhance the success of genetic improvement via selection. For example, the ability to freeze semen and use artificial insemination dramatically increased the ability to identify and utilize the best sires in selection programs. Another example is the development of advanced statistical algorithms to combine complex pedigree and performance information into usable selection criteria such as EDPs; these statistical programs, in combination with dramatic enhancements of computer processing power, have been instrumental in the success of beef cattle genetic improvement programs.

EPDs predict the genetic makeup of an animal. This is successful regardless of the fact that the actual genes responsible for controlling the trait being improved, and more specifically, the different alleles at these genes which make animals superior or inferior, are unknown. However, selection is difficult, expensive and/or time consuming to implement for traits that are: expressed in only one sex (e.g. milk production); expressed late in life; difficult or expensive to measure on a live animal (e.g. carcass quality); or not very heritable (e.g. reproduction). Furthermore, significant amounts of data are required before the EPD accurately predicts actual genetic makeup.

Clearly, the ability to directly evaluate the genetic makeup of cattle, based on evaluation of their DNA at genes controlling economically important traits, could be of tremendous value to increase the accuracy and efficiency of selection. It is important to realize, however, that the use of DNA-assisted selection would be yet another addition to the toolbox of cattle breeders, and not a complete replacement of existing methods and technologies. In other words, using information on the DNA of animals will be an additional resource to tap when trying to identify which are superior and which are inferior cattle. No genetic manipulations are involved, which renders consumer acceptance of this emerging technology essentially a non-factor.

DNA MARKERS II: DNA-ASSISTED SELECTION – CURRENT STATUS

In one sense, DNA-assisted selection is already a reality. In another sense, the widespread use of DNA information in making selection decisions for most economically relevant production traits remains a stubbornly complex, difficult and elusive goal whose shape is still taking form. To understand this dichotomy, one must first comprehend the clear differences between simple (qualitative) and complex (quantitative) traits. For simple traits, usually one gene is responsible for determining the phenotype, and environmental conditions have little or no effect. Examples of such traits include gender, horns, coat color, certain diseases, and rare performance traits (e.g. double muscling). In contrast, complex traits are controlled by many genes (potentially dozens or even hundreds), which can form intricate interactions with each other and with environmental influences such as nutrition, climate and production schemes. Unfortunately, almost all traits of economic significance in cattle production are complex in nature, including growth, body composition, carcass quality, reproduction, milk production and overall disease resistance.

Genetic tests for simple traits are much easier to develop. Indeed, DNA-based selection can already be practiced for many such traits in beef cattle. Embryos may now be sexed based on a simple DNA test. Certain coat color variations (red factor) can be predicted. Various diseases may be diagnosed at the DNA level, including Pompes, DUMPS, beta-mannosidosis, and maple syrup urine disease. Most recently, the gene causing the double-muscling phenotype has been identified (myostatin), and a genetic test can be used to identify positive and negative alleles. These tests identify the actual mutation and/or DNA sequence that directly control each respective trait. Thus, there is no ambiguity and the tests are completely accurate in predicting phenotype.

In regard to complex traits, development of useful genetic testing is still primarily elusive. Evidence from the few powerful studies conducted to date indicate that even for complex traits, it is likely that a few genes may exist that together account for a reasonable percentage of the phenotypic differences between high and low performing cattle. If this is proven to be true, then genetic testing for some complex traits may become a reality in the future. However, it must be emphasized that the widespread application of these tests may be quite limited for some time. This is because it is highly possible that a gene that helps to control a complex trait may have different effects in different breeds and/or in different environments. Thus, for any new genetic test that may be used to help predict breeding value of cattle, research will be needed to evaluate the consistency of the test in different breeds, and across variable environments and management systems.

Despite these complexities, the potential power of DNA-Assisted Selection is enormous. Besides the obvious benefit of increasing the accuracy of selection and decreasing the time required to reach selection decisions, there are additional less obvious payoffs. For example, it is currently difficult to genetically increase intramuscular fat without an accompanying increase in overall carcass fat. However, it is clear that there are individual genes that can influence one trait without changing the other. By focusing selection decisions on targeted DNA information, these negative genetic correlations can be potentially be broken apart to achieve more precise phenotypic improvements.

DNA MARKERS II: DNA-ASSISTED SELECTION – FUTURE

It is likely that significant advances in the tools of genomics will be required to facilitate the discovery of genes controlling complex traits, as well as the affordable use of DNA testing as a widespread and integral tool for beef cattle breeders. However, such advances can be expected. For example, given the successes in determining the complete DNA sequences of humans and mice, it is reasonable to expect that commercial efforts to duplicate these feats will occur in livestock species, including cattle. With the complete genetic blueprint for cattle in hand, much more plentiful and powerful tools for genetic discovery will be available. These discovery tools, when combined with relevant commercial populations and accurate measurement of important phenotypes, may enable identification of genes and development of genetic diagnostic tools for complex, economically relevant traits.

Despite this relatively optimistic view, there is no guarantee that the complexity of the traits and systems that exist in beef cattle production will be sufficiently overcome to enable DNA-assisted selection anytime soon. However, if future research efforts are successful, at some point a scenario may eventually arise in which a breeder can take a hair root from a newborn calf, swish it around in a simple buffer, spread the solution on a glass slide called a "DNA-Selection Chip", insert the chip into a special port on a laptop computer, input data regarding the breeder's particular selection needs (e.g. emphasize marbling and rib-eye area more than weaning weight) and management practices, and rapidly obtain a highly accurate EPD. Unfortunately, in the meantime, one can expect relatively slow progress in the tantalizingly appealing paradigm of DNA-assisted selection.

DNA MARKERS III: DNA-ASSISTED MANAGEMENT

Due to their economic impact, and the difficulty involved in using traditional selection, it is likely that phenotypes such as marbling and tenderness will be the focus of development for the first genetic tests for complex traits. While such tests will certainly be useful in breeding programs, they may be even more beneficial for enhancing the efficiency of management and production systems. For example, carcass quality genetic testing could be used as an efficient sorting tool in feedlots. In addition, it is likely that other management-based DNA tests will be developed in the future, for practices such as selection of implants for maximal response, increasing efficiency of nutritional regimens, and optimizing drug dosage. In the same vein as the "DNA-Selection Chip" may be used to rapidly estimate EPDs, a "DNA-Management Chip" may eventually be used to rapidly determine how cattle should be sorted, treated and managed at various points in the production cycle.

Such management tools may not only enhance production efficiency, but could also lead to quality branded and niche-market (e.g. hormone-free beef) products. However, even if DNA-based management tools are successfully developed, practical implementation of high-throughput DNA-based testing in a feedlot setting or intensive production system represents a significant logistical challenge.

DNA MANIPULATION: GENETIC ENGINEERING AND DESIGNER CATTLE

While DNA-assisted selection attempts to identify the *existing* genetic makeup of cattle to enhance genetic improvement or production management, genetic engineering actually *alters* the genetic makeup of cattle. This distinction is critical in understanding the potential promise (and limitations) of this powerful technology.

Traditionally, genetic engineering was considered as a mechanism to enhance production traits of beef cattle by designing animals that produce more (or less) of proteins that impact important phenotypes. For example, cattle could be engineered to have more growth hormone, potentially increasing lean tissue accretion and efficiency of growth. Alternatively, non-double muscling cattle could be engineered to have mutations in myostatin, resulting in various degrees of increased muscling. One reason why genetically modified organisms (GMO) are not currently, nor will be anytime soon, part of beef production is that the methods used to develop and produce such animals are of low efficiency and high expense. Perhaps more importantly, however, is that our knowledge of how complex traits are regulated, and how they can be successfully manipulated, is still at very embryonic stages. Once we better understand how important phenotypes are regulated in beef cattle, our ability to design animals through genetic engineering will be enhanced.

However, the development of genetically engineered crops such as roundup-ready soybeans and BT-corn showcased the use of genetic modification to create completely novel phenotypes for agricultural organisms. These successes have created a new paradigm for the use of genetic engineering, to design value-added phenotypes dictated by genes that may originate from extremely diverse organisms. This paradigm shift has recently been adopted in research geared towards improving the environmental friendliness of pork production, through development of pigs expressing phytase in their saliva. In this regard, the potential uses of genetic engineering are only limited by one's imagination. For example, a variety of different health-related products could be delivered via "smart beef" (e.g. well-marbled, cholesterol-lowering ribeye). Alternatively, cattle could be engineered to increase the ease and efficiency of management (e.g. through resistance to a variety of pests or diseases).

Perhaps the biggest obstacle to commercialization of genetically modified cattle will be public acceptance. Given the current battle regarding GMO crops, the placement of genetically modified hamburgers in school lunch programs is not presently an appealing notion. However, given that genetic engineering of beef products will likely not be a reality for quite some time, the battle over public acceptance of GMOs will almost certainly be fought and decided on battlefields other than feedlots and meat counters.

SUMMARY AND CONCLUSIONS

Traditionally, the merits and payoffs of DNA-based biotechnology have been oversold to breeders and producers. Expectations of "silver bullets" have come and gone. In reality, the ability to use biotechnology to incorporate DNA information in genetic improvement programs is directly proportional to our understanding of the sciences of

molecular biology, genomics and physiology. As we understand more about the genome and how complex traits are controlled, and as our toolbox of techniques and methodologies grows and improves, we will increasingly be able to enhance genetic improvement of beef cattle as well as the management of beef cattle production and development of high quality beef products. Until recently, progress in this regard was a slog. However, we are currently in the opening throes of a genomics revolution. While exponential successes may be a tall order, we can and should expect more rapid implementation of DNA-based biotechnology in the beef cattle industry than what has occurred in the past.