

Pinard M-H, Gay C, Pastoret P-P, Dodet B (eds): Animal Genomics for Animal Health. Dev Biol (Basel). Basel, Karger, 2008, vol 132, p 327-330.

.....

Opportunities for Collaborative Phenotyping for Disease Resistance Traits in a Large Beef Cattle Resource Population

R.M. Thallman, L.A. Kuehn, M.F. Allan, G.L. Bennett, M. Koohmaraie

US Meat Animal Research Center, USDA-ARS, Clay Center, NE, USA

Key Words: Disease resistance, phenotypes, beef cattle

Abstract: The Germplasm Evaluation (GPE) Project at the US Meat Animal Research Center (USMARC) is planned to produce about 3,000 calves per year in support of the following objectives: identification and validation of genetic polymorphisms related to economically relevant traits (ERT), estimation of breed and heterosis effects among 16 breeds for ERT, and estimation of genetic correlations among ERT and physiological indicator traits (PIT). Opportunities exist for collaboration in the development and collection of PIT phenotypes for disease resistance. Other areas of potential collaboration include detailed diagnosis (identification of disease causing organisms, etc.) of treated animals, collaborative development of epidemiological statistical models that would extract more information from the records of diagnoses and treatments, or pharmacogenetics. Concentrating a variety of different phenotypes and research approaches on the same population makes each component much more valuable than it would be individually.

INTRODUCTION

The USMARC is embarking on an ambitious initiative to study the genetics of disease resistance. The approach is to build a large resource population that is deeply phenotyped for as many traits as possible, with appropriate tissue samples collected at appropriate times for effective and comprehensive study of disease resistance. The general philosophy is that research in the field can proceed more rapidly if samples and phenotypes are readily available for initial studies. Then, based on the initial studies, sampling and phenotype protocols can be adjusted, as needed, to meet specific experimental requirements in subsequent years.

Scientists at USMARC will use this population to conduct research in areas of high priority to our stakeholders, subject to expertise and resources available at

USMARC. Initial efforts at USMARC will be focused on bovine respiratory disease (BRD), because it is the disease with the greatest economic impact on the US beef industry [1]. However, the scope of the problem is obviously too great for the project to be conducted entirely by USMARC. Therefore, we are seeking collaboration with laboratories capable of adding value to the initiative.

The objectives of the initiative are to determine the feasibility of genetic change of disease resistance through selection, identify a suite of phenotypic measures that can be used to indicate clinical and subclinical infections, evaluate variation in these indicator measures, and characterize physiological mechanisms involved in infection and immunological response. These objectives will be assessed through a two-pronged approach of quantitative genetics and functional genomics. The quantitative genetics approach involves the generation of the populations, phenotypes, and genotypes leading to estimation of genetic parameters, QTL discovery, and ultimately marker identification. The purpose of the functional genomics approach is to understand pathogen interactions throughout the process of pathogen invasion leading to host infection followed by the cascade of host response.

MATERIALS AND METHODS

The GPE Project [2] at USMARC is planned to produce about 3,000 calves per year in support of the following objectives: identification and validation of genetic polymorphisms related to economically relevant traits (ERT), estimation of breed and heterosis effects among 16 breeds for ERT, and estimation of genetic correlations among ERT and physiological indicator traits. The ERT include dystocia, survival, growth, carcass, meat quality, feed efficiency, temperament, reproductive, longevity, and maternal traits, as well as records of the diagnoses and treatments of naturally occurring diseases at USMARC. These include bovine respiratory disease, pinkeye, footrot, calf scours, failure of passive transfer of immunity, anaplasmosis, and bluetongue. Other diseases that occur at sufficient frequency at USMARC, or for which we had an occasional outbreak, will also be studied.

The USMARC Disease Resistance Population is a planned subset of the GPE population to be produced by F1 sires via natural service for several years resulting in large paternal half-sib families. It should start at about 600 progeny/yr beginning with the spring 2008 calf crop and increase to about 1,000 progeny/yr by 2010. Phenotyping of this population will be somewhat more invasive (e.g., frequent tissue sampling) than in the other populations described. Feeding of antibiotics will be restricted in this population. Disease-related phenotypes will take higher priority than phenotypes for other trait categories in this population only.

The USMARC Feed Efficiency Population is another subset of the GPE population that consists of animals measured for individual feed intake. It consists of about 2,000 animals through the spring 2007 calf crop and is expected to increase by about 600 to 900 calves per year. At least 300 of these will be measured in a new state-of-the-art feeding facility that allows measurement of feeding behaviour and water consumption in addition to individual feed intake. Additional telemetric technologies for monitoring animal health would be particularly appropriate for study in this population. Serum samples for measuring response to vaccination were collected beginning with the spring 2007 calf crop.

Other cattle populations at USMARC produce about another 3,000 calves per year, all with disease treatment records, DNA samples, and basic weight and production records. Phenotyping for other ERT varies by population. These, and the remainder of the GPE population, can be available for more extensive phenotyping for disease traits, provided the protocols are not too invasive.

About 3,600 USMARC animals, including the current USMARC Feed Efficiency Population and the sires of the USMARC Disease Resistance Population will be genotyped for about 50,000 SNP using the Illumina Infinium BovineSNP50 BeadChip. (Reference herein to any specific commercial products by trade name, trademark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favouring by the United States Government. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government, and shall not be used for advertising or product endorsement purposes.) The USMARC Disease Resistance Population will be extensively genotyped, using state-of-the-art technology, as funding allows.

The plan is to have a variety of different protocols for collecting samples and phenotypes, with less expensive protocols applied to large numbers of animals and the most expensive and invasive protocols applied to fewer individuals.

Disease status should be viewed as an unobservable underlying variable. The objective is that the phenotypes in the following list, when combined properly, would be reasonably effective in predicting disease status. Examples of phenotypes that could be collected at treatment include: veterinary and/or pen rider diagnosis, clinical symptoms, treatment records, temperature, respiration rate, heart rate, pathogen identification and counts from nasal swabs or other relevant tissue samples, immune cell counts and activity, cytokine levels, acute phase protein levels, and antibody titres and activity. Furthermore, lung lesion score may be collected at harvest and necropsy with culture and/or histology of affected tissues performed at death. This list likely needs to be adjusted to be effective and practical, but is provided here as a starting point for discussion. It will only be feasible to apply subsets of the list to most of the populations.

Physiological indicator traits (PIT) are those that are expected to be closely related to physiological processes that are components of disease resistance. In most cases, it should be useful to measure them in all animals in a population, whether sick or not. Ideally, it should be useful to measure them regardless of the level of natural exposure to disease. Because they are related to components, they are expected to have higher heritability than disease resistance itself. Because of higher expected heritability and greater effective numbers of observations than for disease incidence (especially when depending on natural exposure), QTL detection for PIT is likely to be considerably more successful than QTL detection for disease incidence directly. Then, QTL for PIT can be validated for effects on disease incidence in larger populations. The following list of potential PIT is presented as a starting point for discussion: antibody titres and activity, cytokine levels, immune cell counts and activity [3], or other indicators of immune response to naturally occurring diseases or vaccination (including antigens the animals would have no natural exposure to). Other possibilities include quantitative assessment of pathogen load (e.g., worm egg counts), telemetric sensing of body temperature, rumen pH, respiration rate, feeding and water behaviour and consumption, or other parameters indicative of disease status. Furthermore, gene expression, proteomics, and metabolomics are classic examples of physiological indicator traits.

DISCUSSION

Genetic improvement of livestock is highly dependent on reliable and definitive phenotypes. However, phenotypes associated with infectious diseases have not been clearly defined. The complex nature of disease resistance and the lack of acceptable animal challenges for disease resistance have hindered previous research in this area. The number and sizes of cattle herds in research stations is decreasing rapidly. Consequently, most current research on disease resistance of cattle relies on collaborations with commercial producers. Although this can have advantages (e.g., large numbers of animals and concentrating on outbreaks) it often seriously limits the amount of information that can be recorded and samples that can be obtained. The aim of this project is to provide a cattle population in which more intensive studies of components of disease resistance can be conducted.

CONCLUSIONS

Concentrating a variety of different phenotypes and research approaches on the same population makes each individual component much more valuable than it would be individually, because it allows determination of how that component fits into the big picture. Specifically, this work should be integrated with work on thermal stress and other work on animal stress and well-being. However, this concept extends beyond animal disease and stress; the GPE population will be extensively phenotyped for many of the most economically important traits in beef production. Therefore, the economic value of genetic improvement for disease resistance could be estimated directly. Such comprehensive objectives will require the collaborative efforts of experts in animal health, quantitative genetics, and molecular genetics from multiple laboratories.

Opportunities for collaboration exist in the following areas: collection of phenotypes that allow more accurate diagnosis and description of disease states, collection of phenotypes for physiological indicator traits, testing or validation of technologies that provide earlier and/or more accurate detection of disease, and electronic monitoring of physiological parameters such as body temperature, rumen pH, respiration rate, etc. We are eager for advice to make the protocols for phenotype and sample collection more effective and practical. Phenotypes that would help to distinguish between disease resistance and disease tolerance are of particular interest. Collection of gene expression, proteomic, or metabolomic data on large numbers of animals is especially encouraged, as is study of differences in pathogen populations among animals. Studies of pharmacogenetics could be considered. It is possible to apply a limited number of treatments to some of the populations, provided sufficient novel phenotypes are collected in conjunction with the treatments. There are also opportunities for collaboration on genetic epidemiology and/or statistical genetics. Although the word “disease” is used here, similar opportunities exist for studying parasite resistance. Similar opportunities for collaboration exist in swine. USMARC does not conduct challenge experiments in which animals are infected with disease-causing agents; however, a small number of animals can be transferred to other facilities in the US for such studies.

To inquire about a specific potential collaboration, send a brief description of the proposed project to Dr. Mark Thallman (Mark.Thallman@ARS.USDA.GOV).

REFERENCES

- 1 Fulton RW, Cook BJ, Step DL, Confer AW, Saliki JT, Payton ME, et al: Evaluation of health status of calves and the impact on feedlot performance: Assessment of a retained ownership program for preweaning calves. *Can J Vet Res* 2002;66:173-180.
- 2 Wheeler TL, Cundiff LV, Shackelford SD, Koohmaraie M: Characterization of biological types of cattle (Cycle VII): Carcass, yield, and longissimus palatability traits. *J Anim Sci* 2005;83(1):196-207.
- 3 Kelm SC, Detilleux JC, Freeman AE, Kehrl ME Jr, Dietz AB, Fox LK, et al: Genetic association between parameters of innate immunity and measures of mastitis in periparturient Holstein cattle. *J Dairy Sci* 1997;80:1767-1775.

Dr. R. Mark Thallman, US Meat Animal Research Center, PO Box 166, Clay Center, NE, USA 68933-0166
Email: Mark.Thallman@ars.usda.gov