ANIMAL HEALTH SYMPOSIUM II: OPTIMIZING DISEASE RESPONSE MODELING

0076 Understanding animal-to-animal variation in disease management. D. E. Kerr*, *University of Vermont, Burlington.*

A long-term goal of animal health research is to understand causes of animal-to animal variation in innate immune function, such that this knowledge can be applied to breeding, selection, management, or other strategies to generate animals with enhanced disease resistance. Key to this research is an accurate determination of phenotype. However, variation in expression of the phenotype due to differing environmental conditions, including differing physiological states of the animal, confound the ability to accurately compare animal-to animal responses, except under well-defined experimental conditions. The range of infection responsive phenotypes is quite likely dependent on underlying genetic variation that gives much promise to finding genetic markers for use in breeding programs. However, the evolving field of epigenetics suggests that in utero and early life environments can have significant effects on gene expression. Model systems to evaluate variation in the innate immune response may assist in more accurate determination of phenotype to enable detection of genetic or epigenetic biomarkers. These model systems may also be of use in testing immature animals for a prediction of adult performance. An example of a model system is the in vivo endotoxin (LPS) challenge that has been used to identify hyper responder animals. Another approach is the dermal fibroblast model in which substantial animal-to-animal variation has been revealed by how their fibroblasts respond to an in vitro LPS challenge. In this model, the cells are cultured under controlled conditions for several passages to limit environmental effects in an attempt to reveal underlying genetic or epigenetic causes for animal variation. Future studies using these and other model systems, combined with well-controlled disease challenges of extreme phenotypes, will lead to a greater understanding of factors contributing to variation in disease resistance.

Key Words: epigenetics, innate immunity, LPS

0077 Can the genetic selection for improved immune response be tailored to expand the efficacy of disease management interventions. B. Mallard*, *Department of Pathobiology, OVC, University of Guelph, ON, Canada.*

Infectious diseases are costly to all aspects of domestic animal management, care, and well-being across all aspects of husbandry, including companion, food, and sport animals. One aspect of animal health, however, serves as both an intriguing puzzle and an opportunity to exploit the basis for the puzzle. That aspect encompasses the underlying cause for some animals to be devastated by an infecting organism that another might only be minimally affected by. Observations of cattle resistant to natural infections have implied the feasibility of breeding livestock for disease resistance. Studies of pigs selected for antibody- (AMIR) and cell- (CMIR) mediated immune responses have demonstrated increased immune responsiveness, suggesting enhanced protection by both type 2 and type 1 responses, respectively. Additionally, natural or artificial infections of cattle suggest that the production of particular IgM, IgG1, and IgG2 isotypes are important for protecting against pathogens. In fact, IgG1/IgG2 ratios are often used to establish whether type 1 (CMIR) or type 2 (AMIR) responses predominate following immunization or infection. With this in mind, this presentation will address novel aspects of animal-to-animal variability in adaptive immune response, as well as some newer findings in the rapidly expanding area of epigenetics and chromatin modifications, and present both new findings, as well as suggestions for promising areas of research out of which may result better strategies toward maintaining animal health.

Key Words: cattle, immunity, phenotype

0078 Selecting pharmacological interventions through rapid screening motifs and proper cell models. E. Zudaire*, *NIH-NCI, Bethesda, MD.*

There is no doubt that the magnitude and complexity of challenges to pharmacological intervention in disease processes are increasing exponentially. These challenges span all facets of intervention from countering antimicrobial resistance to expanding the pharmacogenomic capacity toward individualizing therapy and prevention. While the drug development landscape is rapidly evolving, current pipelines to approval and applied medicine often rely on well-established compartmentalized research models. In this rubric, targets are first identified in laboratories, frequently on the basis of the now discredited philosophy of "disease-causing" targets. More appropriately, target-specific therapeutics are capable of being designed with the goal of increasing efficacy while better managing undesirable toxicities. However, it has recently been proposed that target-based approaches often fail under clinical trials due in part to the robust nature of networks that control biological processes. The issue is 1 of having the needed target specificity as screenable with high throughput cell-based assessment models, where those models accurately reflect the complexity of in vivo cell-cell interactions and associated gene expression patterns, largely now in evidence in traditional 2D monoculture conditions. The goal is then to connect diseases with underlying pharmacologically tractable targets and drugs that can be translated for their clinical management. To this aim, I will present the case for increasing research into novel technological approaches based on the hypothesis that the most effective therapies for a given disease

would target a complex set of interactions among different components of the system, rather than the activity of a single component. I will expand on how the discovery of effective disease therapeutic modulators requires the development of novel kinds of in vitro assays, which recapitulate the complexity of disease-specific tissue microenvironments.

Key Words: disease, intervention, pharmacogenomics

0079 Managing animal health from an aquaculture perspective. C. A. Shoemaker*, B. R. LaFrentz, D. Xu, and D. Zhang, *USDA-ARS, Aquatic Animal Health Research Unit, Auburn, AL.*

Aquaculture is the production of aquatic animals for food. The aquaculture industry is a rapidly expanding segment of U. S. agriculture and NOAA estimated the industry was worth $1.2 billion in 2011. Disease-related losses in aquaculture either by decreased performance and/or mortality is estimated by the World Bank to be around $3 billion globally. In 1974, Snieszko proposed the host-pathogen-environment relationship theory as applied to fish with regard to development of disease. Age, species, strain(s), nutritional, and immunological status of the host are relevant to disease induction. The pathogen, including exposing dose, virulence, and genetic type (strain), is also pertinent to disease in aquatic animals. For aquatic animals, the environment is probably the most important factor in relation to disease development. Fish are produced in all types of water (i.e., fresh, brackish, and salt water) and fish must rely on water for temperature regulation, oxygen, waste removal, etc., for optimal performance and health. Aquatic animal health management is unique due to the fact that animals are reared in water. Disease can be difficult to discover in water. Once disease is identified, treatment can be problematic because of the size of ponds and/or volume of water. Also, limited treatment options are available due to the fact that few medicines are FDA approved. In some aquaculture operations (e.g., catfish production), all sizes of fish may be raised together in a multi-batch culture. Therefore, separation of healthy and sick animals is challenging. Prevention is the key to successful health management of fish and should include good husbandry practices to limit stress, providing adequate balanced nutrition, use of vaccines, and prudent use of medicines. This presentation will highlight the unique aspects of aquatic animal health management and outline areas where further work may improve our understanding of animal health.

Key Words: aquaculture, fish, health management