The High Immune Response Technology: Breeding Healthier Cows with Improved Immunity

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Identifying dairy cows with superior immune response reduces disease occurrence, increases farm profit, improves milk quality as well as safety, and increases animal well-being. In Canada, it costs the dairy producer $110 to $320 per case of mastitis, and it has been estimated that 1 out of every 5 dairy quarters in Canada is infected with a mastitis-causing pathogen at any given point in time (Canadian Bovine Mastitis Research Network, “What’s New in the World of Mastitis Research?” http://www.medvet.umontreal.ca/rcrmb/dynamiques/PDF_AN/Results/NewspaperWhatsNew.pdf. 2009). The emergence of antibiotic resistant pathogens is of constant concern to the public, and also to livestock producers. Globally, there is a concentrated effort to limit the use of antibiotics and other therapeutics where microbial drug resistance can develop. This is relevant to both human and veterinary medicine. With these concerns in mind, global health agencies are now strongly focussed on disease prevention, not only disease treatment and cure. The current model is in line with the adage that “an ounce of prevention is worth a pound of cure”. Therefore alternative methods for livestock disease control are earnestly being sought around the world where disease prevention is at the forefront. Various genetic strategies have the potential to help with disease prevention and are being assessed as suitable methods to enhance disease resistance of livestock, including dairy cattle. One appealing option currently available for dairy cattle is to make use of the animal’s own inherent ability to make a robust immune response to identify the healthiest animals with naturally superior disease resistance. This approach can work well in either conventional or organic farms. In Canada, the High Immune Response (HIR) technology has been developed to identify and select cattle with improved resistance to a broad range of pathogens, including those that cause mastitis.

Genetic Regulation of the Immune System and Disease Resistance

The immune system is a collection of genetically regulated cells and molecules that control the response to disease causing micro-organisms, including those that cause bovine mastitis. Improved understanding of genetic regulation of the immune system has led to a patented method to identify dairy cattle with inherently superior immune responses. Studies by
Professor Mallard and her group in Canada have focussed on evaluating host defence mechanisms as indicators of specific and broad-based inherent disease resistance. In fact, cattle can be identified as having high, average or low immune responses, and the “high responders” have better resistance to a wide range of infectious diseases. In most species, including cattle, the heritability of immune responses (i.e. the genetically inherited component of the trait) are sufficiently high to allow for improvement via genetic selection. Early research by the Mallard group showed health and production benefits following genetic identification of both cattle and pigs with increased immune responses. In dairy cattle, this included lower occurrence of mastitis in high immune responders in 2 out of 3 Canadian herds tested, as well as improved response to vaccination and colostrum quality. A more recent study of 58 dairy herds that were part of the Canadian Bovine Mastitis Research Network (CBMRN) also indicated that cows identified as having high immune responses had lower mastitis incidence that was of lower severity than cows classified as average or low responders. This included the incidence of both E. coli and S. aureus mastitis. Another study on a large US dairy substantiated these claims by demonstrating reductions in mastitis, ketosis, metritis and retained placenta incidence of cows with both high antibody and cell-mediated immune responses compared to average or low responders based on their estimated breeding values for these traits. In general, the reduction in mastitis incidence in high immune responders was about 20% which represents a substantial cost saving to the producer. The individuals with both higher and more optimally balanced antibody and cell-mediated immune responses (two critical factors involved in immunity) are referred to as “High Immune Responders”, and the test system is known as the 

High Immune Response (HIR) technology. The HIR test can be used to immune response phenotype dams, sires or calves as early as 2 months of age or older. Since the immune response traits used in the HIR test have heritability values similar to that of milk production traits (~25%), it is possible to make genetic gains in immune response relatively quickly, as has been the case for various production parameters.

Using this quantitative genetic method to identify and select individuals with higher breeding values for immune response traits is a novel genetic tool that does not require molecular genetic information or manipulation of the animal and therefore avoids current controversies surrounding production of genetically modified organisms (GMOs). Nonetheless, the advantages of modern molecular genetic techniques are being employed at the laboratory level to identify and study favourable animal genotypes. In fact, the Illumina SNP 50K bovine BeadChip has been utilized to evaluate difference in cows with high or low antibody-mediated immune responses. In this study, 198 genes that are part of 11 genetic pathways were shown to differ between these cows. Although there is still more research to be done in the genomics arena, it does suggest that in the future it may be possible to identify high or low immune responders from a simple DNA sample.

Immune Response and Production

To date, results from the Mallard lab over multiple studies have shown that breeding for high immune response based on both antibody and cell-mediated immune responses would not compromise production traits, and indeed may improve overall herd life. It was also worth noting that when relative immune response breeding values of sires were calculated from the
CBMRN study that there were beneficial associations noted between immune response and breeding values of sires for herd life, as well as between high cell-mediated immune response and milk yield.

**Practical Implication of the High Immune Response (HIR) Technology**

Breeding companies distribute sire proofs (breeding values) to improve mastitis that include somatic cell score (SCS), and in some countries clinical mastitis, as indicators of udder health. These indicators however, focus only on one disease, whereas HIR focuses on general broad-based disease resistance. The HIR test measures both antibody and cell-mediated immune responses that possess the characteristics of pathogen specificity and immunological memory that allows the individual to produce a quicker and more rapid response on second and subsequent exposure to the infecting agent. In some cases, these two types of adaptive immune responses can produce lifetime immunity. Breeding companies in Canada, such as the Semex Alliance, are increasing their focus on health traits. In conjunction with the Canadian Dairy Network and CanWest Dairy Herd Improvement (DHI) they are collecting information on eight economically important diseases, recorded by producers on a voluntary basis; mastitis, displaced abomasum, ketosis, milk fever, retained placenta, metritis, cystic ovaries, and lameness (Koeck et al 2012). They have also been supportive partners in the development of the HIR technology for dairy cattle. Organizations such as CanWest DHI also provide information on SCS and bacterial colony forming units in individual milk samples, as well as offer diagnostic milk ELISA tests for *S. aureus* mastitis, Johne’s Disease, and Bovine Leukosis Virus. Some nutrition companies offer rations that support the performance of the immune system, while pharmaceutical companies market and distribute vaccines that prevent respiratory and gastrointestinal infections in cattle, and Gram negative intramammary infections in lactating cows. These are all important tools that support animal health and they work well in conjunction with the HIR technology that is unique in its design to improve resistance to a diverse range of economically important pathogens. This ultimately translates into increased dairy food quality and safety for the consumer, as well as improved animal well-being.
HIGH IMMUNE RESPONSE (HIR) ANIMALS ARE NATURALLY IMMUNE

HIR is a patented evaluation technology developed to identify dairy cattle that have high adaptive immune response capability.

Identification is safe, fast and effective.

Benefits include:

- Lower disease occurrence and severity
- Reduced treatment and veterinary costs
- Increased response to vaccines
- Increased colostrum quality
- Cattle as young as 2 months or older can be tested
- Animals only need to be tested once in a lifetime
- Testing is safe and does not interfere with other diagnostic testing
- Cost benefit analysis show significant savings to producers who identify HIR cows and use HIR sires in their herd.
- HIR is both a management and breeding tool that can be used to improve health in future generations of dairy cattle