Immunity+™
Disease Resistant Genetics

Frequently Asked Questions

Answers sourced from: Jay Shannon, Semex Global Dairy Solutions Manager; Dr. Bonnie Mallard, Professor of Immunogenetics, University of Guelph; Dr. Jacques Chesnais, Semex Senior Geneticist

Q: ***Could the increase in disease incidence as cited by NAHMS from 1997-2007 be more related to better recording of disease data resulting from attrition in the dairy industry?***

A: The NAHMS study (National Animal Health Monitoring System) is a controlled study in the United States conducted every five years on dairies where disease monitoring and data collection are well managed. It would therefore appear the reported rise in disease incidence is real during the reported time period. There were several earlier reports (E.g. Emmanuelson U., et al., Genetic parameters for clinical mastitis, somatic cell counts and milk production estimated by multiple-trait restricted maximum likelihood. JDS 71:476, 1988) that indicated heavy selection for production with little or no emphasis on health traits was associated with increasing disease. The dairy industry has been trying to address that problem by including various health traits in the current selection strategies. Nonetheless, there is no doubt that disease is a large and costly problem to the dairy industry. Additionally, health issues can create problems, real or perceived, with food quality and safety for the dairy industry.

Q: ***Has the skin thickness test to assess cell-mediated immune response been validated in comparison to cell biopsies?***

A: Yes, this work was done by one of Professor Mallard's students, Dr Armando Hernandez-Heriazon (DVM, PhD). The work appears in his graduate thesis and was also published in the Journal of Dairy Science. The HIR (high immune response) skin test has been carefully verified to represent true delayed-type hypersensitivity (DTH), with recruitment of T-lymphocytes and macrophages, as a valid indicator of cell-mediated immune response.

Q: ***At what age can an animal be tested? Is there a lower and an upper age limit?***

A: Animals can be tested at two months of age or older. This minimizes maternal antibody effects.

Q: ***Can a list of diseases be provided based on their association to cell-mediated or antibody-mediated immune response including those validated by research and those not yet validated?***

A: It is well established that both antibody and cell-mediated immunity work together to control disease, and there are plenty of examples to demonstrate that antibody (of the correct isotype) is critical to control extra-cellular pathogens, such as E. coli and S. aureus. On the other hand, cell-mediated immune responses are critical to the control of intra-cellular pathogens, such as virus and facultative intracellular bacteria (refer to Table 2 below).

We recommend the following books on this subject:

Immunology, by Dr Richard A. Goldsby et al. In the first few chapters of this text it explains the role of humoral and cellular immunity. The cytokine chapter also explains the role of T-helper 1 and 2 responses and how these distinct profiles drive antibody and cell-mediated immunity to provide protection to intra- and extra-cellular pathogens, respectively.

Veterinary Immunology by Dr Ian Tizzard. This is also an excellent resource on the topic.

Table 2. Both antibody and cell-mediated immunity are important in pathogen control, although antibody tends to predominate in control of extra-cellular pathogens; whereas, cell-mediated immunity is critical to control of intra-cellular pathogens.

Extra-cellular Pathogens known to induce Antibody-mediated Immune Responses	Intra-cellular Pathogens known to induce Cell-mediated Immune Responses, such as Delayed-type Hypersensitivity
E. coli (including mastitis causing strains)	Mycobacterium (tuberculosis and paratuberculosis)
S. aureus (including mastitis causing strains)	Listeria
Streptococcus	Brucella
Closteria	Leishmania sp.
Diptheria	Histoplasma
Bordetella	Crytococcus
Haemophilus	Influenza and other virus

Adapted from Immunology by Goldsmith et al. and printed by W.H. Freeman and company (chapter on immune response to infectious disease).

Q: ***Ketosis has sometimes been listed as one of the diseases Immunity+ can impact. Does Immunity+ having an effect on ketosis?***

A: One aspect of Immunity+, antibody-mediated immunity, was associated with a reduction in the relative incidence of ketosis in the Florida data. However, because the incidence of ketosis in that herd was small, the effect, even though it was large, was not statistically significant. As a result, it is not shown on current Immunity+ documentation. Some have questioned whether immune response could impact the incidence of ketosis since it is a metabolic disease. One possible answer is that many recorded diseases tend to have positive genetic correlations with each other (i.e. animals that are in poor health tend to suffer from more than one disease, even if these diseases have different causes). This has been shown in both US and Canadian studies (Zwald N. et al., JDS 87:4295-4302, 2004; Koeck A. et al., JDS 95:4099-4108, 2012), and could explain why Immunity+ has an effect on diseases other than those directly linked to infectious pathogens. A definitive answer to the ketosis question, however, will require the collection of additional data in herds where the incidence of ketosis is relatively high.

Q: ***Is the lower incidence of sero-positive low cows for high cell-mediated immune response cows relevant considering the poor sensitivity and specificity of the serum ELISA test for Johne's disease?***

A: Although this is not the best diagnostic test, it is the only test available at the moment for Johne's. Until something better is available, this test is still considered to be the gold standard and is used in the US and Canada. Further research is needed to verify the results from this study reported by Pineto et al 2009. Nonetheless, these results fit very nicely with the fact that disease caused by mycobacterium are best controlled by cell-mediated type I immune responses, such as delayed-type hypersensitivity, measured and used to classify cows in this study.

Q: ***How many animals (cows and heifers) have been tested for immune response under this research?***

A: In the studies shown during this presentation, approximately 2000 cows from 64 herds were tested in five independent studies conducted over several years. Disease data was collected by trained technical staff or herd veterinarians and provided to the researchers only after immune response classification was complete.

Q: ***There were 700 cows out of 3,000 cows at one herd in Florida. How many were high immune cows and how were these 700 preselected?***

A: The 700 cows were randomly selected from the herd for immune response testing. Those that were one standard deviation above and below the population mean were classified as high or low responders, respectively. This study was published in the Journal of Dairy Science.

Q: ***In stating that the heritability of immune response is 25%, how do you quantify the combined passive, innate, and acquired immune response in order to determine the heritability?***

A: The heritability for antibody and cell-mediated immune responses has been determined through various studies, with 25% being the average over all studies conducted by the Mallard group for dairy cattle. Similar heritabilities were also reported for these traits in pigs and other species. It is very clear from all of the literature that the heritability for adaptive immune responses is moderately high.

Innate defense mechanisms are varied and numerous. The HIR technology captures those important in initiation and activation of specific antibody and cell-mediated immune responses.

Q: ***For the comparison that showed higher quality colostrum for high immune response cows, did they test the colostrum itself or the calves? How did they test it over these weeks?***

A: Colostrum was considered to be a "milk" sample taken not later than 48 hours after calving. Samples were aliquoted into several small vials and stored frozen until the time of testing. Specific antibody was measured by ELISA. Subsequent measures of antibody levels were performed on milk taken at various weeks relative to calving. This work was published in the Journal of Dairy Science. These results were subsequently verified in a 2012 study that is currently being prepared for publication. Not surprisingly, calves receiving colostrum with greater amounts of antibody also showed more antibodies in their serum.

Q: ***For the comparison showing the higher response to commercial vaccines for high immune cows, when was the vaccine administered? Why does the graph begin at week -8 and go to week +6?***

A: In this particular trial, the sampling period was from dry off (week -8) throughout the peripartum period (weeks -3 to +3 relative to calving) and concluded at week 6 post-calving. The objective was to both classify cows for immune response and to evaluate their response to a J5 E. coli vaccine given at week -8, -3 and 0 relative to calving. This research was published in the Journal of Dairy Science.

Q: ***Is the additional value of $80 based upon an average with heritability factored in or is this only for daughters of HIR bulls that would test as HIR cows?***

A: The $80 value takes into account the heritability of immune response. Essentially the calculation is based on the genetic superiority of the bulls (based on their selection intensity, which is approximately 10%, and the heritability of the trait, which is 25%). Daughters receive half their genetic superiority of their sire. The economic calculation is then based on the superiority of the daughters for immune response, its impact on health traits based on the research work carried out by Dr Mallard's team, over three lactations, and the cost associated with each disease occurrence (based on estimates from the literature). The approach for computing economic value is very similar to that used for Net Merit (economic value expressed in the daughters, for three lactations).

Q: ***Are Immunity+ genes dominant or recessive?***

A: There are over 2000 genes that control host defense. Consequently, at this time we have not evaluated the effect of dominant versus recessive. This information is also not relevant to being able to improve immune response using the HIR technology. The immune response variables measured in this method are continuous traits with moderately high heritability, similar to that of milk production and all other quantitative traits we select for today. Genetic improvement will accumulate in the same way as for these other traits, which are all controlled by many genes.

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