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Genetic variability in the humoral immune response to bovine herpesvirus-1 infection in dairy cattle and genetic correlations with performance traits

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ABSTRACT

Bovine herpesvirus-1 (BoHV-1) is a viral pathogen of global significance that is known to instigate several diseases in cattle, the most notable of which include infectious bovine rhinotracheitis and bovine respiratory disease. The genetic variability in the humoral immune response to BoHV-1 has, to our knowledge, not ever been quantified. Therefore, the objectives of the present study were to estimate the genetic parameters for the humoral immune response to BoHV-1 in Irish female dairy cattle, as well as to investigate the genetic relationship between the humoral immune response to BoHV-1 with milk production performance, fertility performance, and animal mortality. Information on antibody response to BoHV-1 was available to the present study from 2 BoHV-1 sero-prevalence research studies conducted between the years 2010 to 2015, inclusive; after edits, BoHV-1 antibody test results were available on a total of 7,501 female cattle from 58 dairy herds. National records of milk production (i.e., 305-d milk yield, fat yield, protein yield, and somatic cell score; $n = 1,211,905$ milk-recorded cows), fertility performance (i.e., calving performance, pregnancy diagnosis, and insemination data; $n = 2,365,657$ cows) together with animal mortality data (i.e., birth, farm movement, death, slaughter, and export events; $n = 12,853,257$ animals) were also available. Animal linear mixed models were used to quantify variance components for BoHV-1 as well as to estimate genetic correlations among traits. The estimated genetic parameters for the humoral immune response to BoHV-1 in the present study (i.e., heritability range: 0.09 to 0.16) were similar to estimates previously reported for clinical signs of bovine respiratory disease in dairy and beef cattle (i.e., heritability range: 0.05 to 0.11). Results from the

present study suggest that breeding for resistance to BoHV-1 infection could reduce the incidence of respiratory disease in cattle while having little or no effect on genetic selection for milk yield or milk constituents (i.e., genetic correlations ranged from -0.13 to 0.17). Moreover, even though standard errors were large, results also suggest that breeding for resistance to BoHV-1 infection may indirectly improve fertility performance while also reducing the incidence of mortality in older animals (i.e., animals >182 d of age). Results can be used to inform breeding programs of potential genetic gains achievable for resistance to BoHV-1 infection in cattle.

Key words: bovine herpesvirus-1, infectious bovine rhinotracheitis, bovine respiratory disease, animal health

INTRODUCTION

Infectious bovine rhinotracheitis (**IBR**) is a contagious viral respiratory disease of cattle caused by infection with bovine herpesvirus-1 (**BoHV-1**). Listed as a notifiable disease by the World Organization for Animal Health, IBR is of global importance and may even be considered a disease of trade, especially within the European Union (**EU**). Several countries and regions have achieved an IBR-free status according to Article 10 of EU Council Directive 64/432/EEC, whereas others have approved eradication programs according to Article 9 of the same Directive. In both cases, Commission 2007/584/EC grants them additional guarantees with respect to trade with other member states of the EU. Furthermore, Council Directive 2003/43/EC prohibits the entry of bulls with BoHV-1 antibodies to bovine semen collecting centers in member states or third countries where semen is collected for intra-community trade or import to the EU. Cowley et al. (2011) reported that 74.9% of Irish dairy and beef herds were sero-positive for BoHV-1. Although no national IBR control or eradication program currently exists in Ireland, Animal Health Ireland (www.animalhealthireland)

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.ie) is currently developing the technical and business case for such a program.

Clinical signs of IBR in cattle include reduced appetite (Muylkens et al., 2007), elevated body temperature (Thompson et al., 1965; Muylkens et al., 2007), conjunctivitis and inflammation of the nares and trachea (Thompson et al., 1965), reduced milk production (Hage et al., 1998), compromised reproductive performance (Graham, 2013), and death (AFBI and DAFM, 2016). Bovine herpesvirus-1 infected animals are also predisposed to secondary infections (Yates, 1982). The severity of clinical signs arising from BoHV-1 infection vary depending upon the immune status of the animal (Muylkens et al., 2007) and the virulence of the BoHV-1 strain (Kaashoek et al., 1996). Infection with BoHV-1 for the very first time (i.e., primary infection) typically results in clinical signs and the shedding of BoHV-1 (Engels and Ackermann, 1996). Following primary infection, animals become latently infected, no longer exhibiting clinical signs, synthesizing or shedding BoHV-1 (Engels and Ackermann, 1996), but continuing to harbor the virus in their nervous system (Muylkens et al., 2007). These latently infected animals have the potential to reactivate and re-excrete BoHV-1 (Geraghty et al., 2012), generating new primary infections during periods of stress, corticosteroid treatment, or when re-exposed to circulating BoHV-1. Latently infected animals are lifelong carriers of BoHV-1 and potential transmitters of the virus between herds. Transmission of BoHV-1 can also occur by airborne spread, use of semen from infected bulls, or through the use of contaminated equipment or clothing.

To our knowledge, no study has attempted to quantify the genetic variability in the humoral immune response to BoHV-1 in dairy cattle or its association with performance. However, evidence of genetic variability in the prevalence of clinical signs to other viral diseases in cattle does exist. Muggli-Cockett et al. (1992) identified breed differences among 9 purebred and 3 composite beef breeds in clinical signs of bovine respiratory disease (**BRD**) with Braunvieh and Pinzgauer breeds exhibiting a greater prevalence of BRD than the other purebred and composite breeds. Heringstad et al. (2008) also reported a heritability estimate for BRD of 0.05 in a population of Norwegian Red calves, although in that study BRD was unlikely to have been caused by BoHV-1 because the Norwegian cattle population is deemed free of IBR (Heringstad et al., 2008).

The objective of the present study was to quantify the genetic variation present among Irish dairy cattle females in their humoral immune response to BoHV-1 and the genetic association of humoral immune response to BoHV-1 with milk and fertility performance

traits as well as animal mortality. Results can be used to determine the feasibility of genetic selection in cattle for enhanced resistance to BoHV-1 through either selection for resistant breeding animals or exclusion of susceptible animals from breeding stock. Furthermore, results can be used to determine if current breeding goals for performance traits may be influencing the humoral immune response to BoHV-1.

MATERIALS AND METHODS

Data

The BoHV-1 data originated from 2 Irish sero-prevalence studies undertaken by the Animal and Grassland Research and Innovation Centre, Teagasc, Moorepark, Fermoy, Co. Cork, Ireland, between the years 2010 and 2015, inclusive. National records of milk production performance and fertility performance were also available from the Irish Cattle Breeding Federation (**ICBF**) database for the years 2010 to 2015, inclusive. Furthermore, national animal mortality records were available from the ICBF database for animals that were born between the years 2001 and 2015, inclusive.

BoHV-1 Data

One BoHV-1 data set originated from a sero-prevalence study of BoHV-1 conducted between October 2010 and February 2013, which consisted of 6,534 female cattle from 24 dairy herds. Herds that participated in the study were Teagasc research farms or participants in the Dairy Management Information System, a system that collates producer-recorded stock, farm inputs, production, and reproduction information (Crosse, 1991). The average number of cows per herd over the study period was 193, ranging from 71 to 758 cows. Holstein, Jersey, Norwegian Red, and Friesian were the main breeds, accounting for 96% of animals. Blood samples were collected from each animal at least once during the 4-yr period and tested for the presence of BoHV-1 antibodies. Each herd's vaccination history for each year was also collected. The only information available pertaining to herd-level vaccination status was whether the herd was either not vaccinating or vaccinating with a marker vaccine; information on the frequency of vaccination or the type of vaccination used (i.e., live or inactivated vaccine) was not available. Herd-level vaccination status was used to interpret the test kit used for detecting animal-level BoHV-1 antibodies. Currently, 2 types of test kits are available to detect BoHV-1 antibodies (i.e., gB and gE test kits). Marker vaccines, non-marker vaccines, and field virus

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