GWAS of resistance to paratuberculosis in French Holstein and Normande cattle breeds

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A case-control genome-wide association study (GWAS) was applied to identify QTL of resistance to Mycobacterium avium ssp. paratuberculosis (MAP) infection in French Holstein (HOL) and Normande (NOR) cattle. Cases were infected shedder cows (confirmed with both positive blood ELISA and fecal PCR) or clinical cases. Controls included animals with 3 repeated negative blood ELISA, negative fecal PCR test, at least 72 months old and born in the same herd and at the same time period as cases. A total of 405 NOR (210 cases / 195 controls) and 989 HOL (437 cases / 552 controls) cows were genotyped with the Illumina BovineSNP50 BeadChip. GWAS was conducted within breed with GCTA, accounting for the population structure through a 50K-based genomic relationship matrix. The most significant region associated with infectious status was found on chromosome (BTA) 12 at 69.8 Mb ($P<2E^{-8}$) in HOL cows. Another association was identified on BTA23 in the region of the major histocompatibility complex (MHC) in both breeds. Other chromosomal regions ($P<7E^{-5}$) were found on BTA1 (55 Mb), BTA10 (91 Mb) and BTA13 (56.6 Mb) in HOL and on BTA1 (92.6 Mb), BTA9 (39.3 Mb), BTA15 (58.4 Mb) and BTA17 (8 Mb) in NOR cows. Seven additional regions were found with more moderate significance level ($P<1E^{-4}$) in NOR (BTA13 and 25) or HOL (BTA3, 9, 11, 25, 26 and 28) cows. This on-going study presents encouraging results. After collecting and genotyping additional cases and controls, whole genome sequences of the cows will be imputed using the 1000 bull genome reference population and GWAS will be carried out directly on whole genome sequence data to pinpoint candidate mutations. This study was funded by INRA (GISA), Apisgene, and GDS France. The authors thank the farmers and GDS who contributed to this project.

Unravelling the contribution of host genetics to infectious disease outbreaks

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Genetic analyses of infectious disease data usually focus on disease resistance. Increasing evidence however shows that risk and severity of disease outbreaks also depend on host infectivity (ability to transmit infections) and tolerance to infection. Estimating genetic parameters for these traits has proven difficult, because current quantitative genetics methods fail to account for the infection dynamics and dependence between traits. Our studies aimed to develop statistical methods to estimate additive genetic risk and SNP effects associated with resistance, tolerance and infectivity. These tools were applied to simulated and real data to gain novel insights into the host genetic contribution to infectious disease spread and impact in livestock populations. When applied to epidemiological data, our dynamic social effects models produced reliable estimates of additive genetic risks and SNP effects for both host susceptibility and infectivity. Prediction accuracies in simulations were above 0.5 and 0.4 for susceptibility and infectivity, respectively, even when information on time-to-infection is imprecise. Informed by these simulations, a large-scale infection experiment in turbot was designed, and revealed that infectivity is heritable and likely genetically correlated with resistance and tolerance. Furthermore, in order to disentangle the relative importance of resistance and tolerance to host responses to infection, we derived a theoretical expression to estimate relative contributions of both traits to the overall genetic variance in host responses. When applied to growth data in pigs infected with PRRS virus, resistance and tolerance were estimated to have similar contributions to the genetic growth variance under infection. Our results offer new opportunities and challenges for implementing novel disease traits into genetic disease control strategies.