Working together to tackle emerging livestock diseases

MITIGATING THE IMPACT OF LSDV & ASFV

African swine fever (ASF) and lumpy skin disease (LSD) are both internationally spreading, infectious animal diseases that pose ongoing threats for European livestock and wildlife. The dynamics of how infectious diseases generally spread between animals is illustrated in Figure 1 (Bishop and Woolliams, 2010). In all these stages of the transmission of infection we can observe variation among animals in how they respond to the infection challenge.

When this variation between animals has a partial genetic background, we can select for animals that can cope better with future outbreaks of these diseases. For example, there is clear host variation in response to LSD infection: in field studies between 30-50% of the animals develop no clinical signs when a herd is infected with LSD virus (EFSA et al., 2020). This was confirmed by experimental challenges where animals were artificially infected (Haegeman et al, 2021). For African swine fever, some pigs recovered from infection with a virulent strain after being immunized with a low virulence strain ('attenuated virus') while other pigs had severe disease and needed to be euthanized (Goatley *et al.* 2022). In Defend, we took a closer look at potential genetic variation behind these observed differences.

Key Achievements

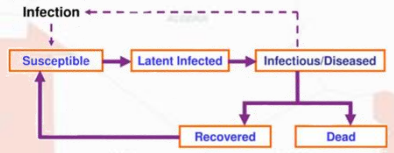

Figure 1. Model for transmission of bacterial or viral infections.
doi:10.1371/journal.pone.0008940.g001

For LSD we looked at genetic variation at two different levels: 1) a population study where we looked at variation in the DNA of the animals in relation to whether they showed clinical symptoms and 2) An experimental study where we looked at the variation in the expression of different genes in relation to the disease outcome and disease progression (Banabazi et al. 2023a).

In the first study we looked at a group of about 200 cows from different participant countries. All these animals had been exposed to the LSD virus but only about 50% of them had developed clinical symptoms. When comparing these animals for about 50 000 known variants in their genomes, we identified two distinct regions in the cattle genome that made a modest, but significant, contribution to the animals being resistant to LSD infection.

In the second study, we compared the complete gene expression profile in the blood of experimentally infected animals at different time points before and after infection. In this study, done twice with animals from Belgium and the UK, we learned that the gene expression response in the cow following infection is strongly dependent on the virus strain that was used for the infection.

While there are some clear expression differences between animals that develop clinical symptoms and those that stay apparently healthy, even these differences are mostly specific for each virus strain. Among the genes that differentiate animals that develop clinical symptoms from those that do not, there are a few interesting genes that show this difference already before the actual infection. Looking at the joint results, we conclude that resistance against LSD has a clear genetic component.

In African swine fever we also looked at the complete gene expression profile in the blood of experimentally infected animals at different time points before and after infection (Banabazi et al. 2023b). Five of the twelve pigs that were immunized with a low virulent strain of the virus, recovered after the infection with the virulent strain. There was a clear difference in the gene expression profile of these pigs compared to those that did not recover. Also here, some of the genes that differed between the recovered and non-recovered animals already showed this difference in expression before the actual infection with the virulent strain. Furthermore, for one gene of interest, the five recovered pigs exclusively shared a mutation in a neighbouring gene that was previously shown to regulate the expression of this gene.

Based on what we have learned from the field- and experimental data, we did a 'thought experiment' on how we could improve resistance against these diseases using genetic selection. Focussing on cattle and LSD we mimicked a breeding structure that is typical for the countries where LSD is endemic: the main cattle breeding efforts take place in a technically sophisticated nucleus herd from which genetically superior animals are spread to the different national herds. This simulation study showed that selection for increased resistance in the nucleus herd can also improve resistance in the national herds, but only if the farmers that own these herds are also interested to select for resistance rather than production only.

Recommendations

In our work package, we have shown that there is genetic variation in susceptibility to LSD and ASF that warrants further research investment. An important component to future genetic studies and breeding initiatives is access to relevant data and samples. This mean that data and sample collection programs must be implemented at the (inter-) national levels to turn disease outbreaks into research and development opportunities. The data that is collected in this manner, can also provide field data to train predictive models for genetic resistance based on a combination of disease status and DNA information. During farm visits for disease surveillance, veterinarians document general data about farm size and proportion affected and take tissue samples for DNA isolation from both healthy and sick animals in a balanced manner. For each animal, the disease status and symptoms should be documented, as well as their age/parity and vaccination status. There are several options where samples for DNA isolation can be stored and transported at room temperatures, greatly simplifying the logistics for using filed samples: hair roots, blood samples on filter paper and nose swabs all can deliver good quality DNA without the need for cold storage.

References

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Background map indicates Global spread of ASFV. In orange are the countries which had ASF in 2018, and in purple are the countries which have reported their first outbreak since 2018.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 773701