

Genetic Defects – Innate Immunity

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Background and Objectives

Recent studies in various laboratories indicate that genetic background can affect resistance of pigs to some infectious diseases. For example, the immune response varies among genetic lines (1), and illness associated with the PRRS virus or porcine circovirus varies among offspring of different breeds or sire lines (2,3). Our research group is looking for genetic defects that make pigs more likely to get sick or die when exposed to various common bacterial and viral infections. We have focused on innate immune proteins, especially mannan binding lectin (MBL), that provide a first line of defence against agents responsible for respiratory or systemic infections (4). In humans, lack of MBL increases susceptibility to various bacteria and viruses (see 4). MBL and similar lectins (e.g. ficolins and lung surfactant proteins) are innate immune proteins that can bind to sugar patterns on the surface of various bacteria and viruses (4).

Recent studies in our group have identified single-nucleotide polymorphisms (SNPs) that demonstrate there are genetic differences in porcine genes for pig MBLs, ficolins and lung surfactant proteins. SNPs that substantially impair function or supply of these lectins are considered to be genetic immune defects that might impair growth or health in some conditions. DNA tests for these SNPs have been developed and used to assess their role in susceptibility to disease.

Defects in porcine mannan binding lectin (MBL) genes

Pigs produce MBL-A and MBL-C mainly in the liver (5). Pig MBL-A in blood binds various bacteria that cause respiratory infections in pigs (5). One SNP in the MBL-A gene is in a location (MBL-A 271 G>T) that could disrupt the assembly of MBL-A. This SNP was found in various breeds and was more common in pigs that were culled with pneumonias and systemic infections (6). However, differences in SNP frequency between healthy and diseased pigs were not large enough to expect substantial improvements by avoiding breeders that carry it (8).

By comparison, a proportion of healthy pigs in all major commercial breeds produce very small amounts of MBL-C (6-8). We found that expression of the MBL-C gene was markedly reduced in pigs that were culled for post mortem diagnosis of various respiratory or systemic infections. Low production of MBL-C was associated with two unlinked SNPs located in the promoter region of the MBL-C gene (7). Pigs with one copy of the defect had several fold reduction in expression whereas pigs with two copies were more markedly deficient. One of these promoter SNPs, namely G(-1081)A, present in approx 25% of healthy pigs, was significantly more frequent in pigs that were culled for various common infectious diseases. A second MBL-C promoter SNP, namely C(-251)T, had a less pronounced impact on MBL-C expression, but the effect was additive with that of the G(-1081)A SNP. The C(-251)T defect was more common and found in the of over 60% of healthy pigs, but was more frequent in cull pigs with various infectious diseases. Promoter polymorphisms similar to those we have found in association with low MBL-C production and disease in pigs are similar to some implicated in innate immunodeficiency and disease susceptibility in humans (4).

Conclusions

DNA-based tests for SNPs associated with impaired production of MBL-C and increased likelihood of disease in pigs have been developed. Such PCR tests are now being used to determine if these and other lectin gene SNPs are useful genetic markers for innate immune deficiency in pigs.

Those correlated with poor growth and ill health in pigs under commercial production conditions could be used to identify breeders that do not have the defects.

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References

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