English Setter immunity genes

In response to a request from your Health Committee, Dr Lorna Kennedy from the University of Manchester has written a short report on her research into health conditions in setters that are associated with the immune system. Because this report is (of necessity) pretty technical, Linda Taylor has asked me to write a brief 'summary' of the main points that emerge. The full report will be posted on the ESA website.

Recent advances in genetics (especially of mankind) have shown that some diseases are under direct genetic control: examples would be cystic fibrosis, haemophilia and Huntingdon's disease. Others are almost entirely 'environmental': if you get bitten by a rabid dog, you might get rabies; if you don't, you probably won't. It is now becoming evident, however, that there is an array of diseases that lie in the middle. If you have a particular genetic make-up, you are susceptible to a disease, but there may well be an environmental 'trigger' that precipitates the illness. This trigger might be something in the environment such as diet (cereals in gluten intolerance) or exposure to a chemical (e.g. asbestos or cigarettes). Alternatively, it might be a viral infection (e.g. measles) that precipitates the illness.

Researchers have discovered that one region of the human DNA can be particularly important in these conditions, and this is the region called the 'Major Histocompatibility Complex' or MHC. The genes associated with this region produce proteins that interact with the white blood cells to generate immunity; they can recognise 'foreign' material (such a bacteria or viruses) and produce antibodies to destroy the invading material, and protect the individual from further infection. They are also involved in tissue transplantation since a kidney or heart from another individual will probably be genetically different, and so be treated as 'foreign' and rejected. It has become increasingly clear that many human diseases show associations with the MHC. If you have a particular genetic constitution at your MHC then you may (*may*) develop a particular disease. If you don't, then you almost certainly won't. Determining the 'trigger' that sets off the disease is the $64,000 question, and vast amounts of money are being spent in laboratories and hospitals around the world to try to identify these.

Just as with humankind, so it is with dogs. There is an MHC region in the canine genome and researchers like Lorna are striving to identify associations (and potentially the causes) of immune-related diseases that are linked to this. There are several different regions within the MHC complex, one of which (Class II) seems to be especially important in immune disease. Class II comprises three main genes, and there are many alternative forms (alleles) at each of these genes. Almost all of us have a different combination of alleles at these three genes, which is why it is so hard to find suitable donors for organ transplants. The more closely related two individuals are, the more likely they are to be a genetic match for a transplant. Identical twins are perfect, siblings less so, cousins even less, and so on. Dogs, too, are very variable ('hypervariable' is the technical term used), though individual breeds are less so because of the inbreeding that has occurred during their development. Lorna has identified over 300 different genetic combinations ('haplotypes') among dogs, and has found that English Setters include only ten of these, five of which are so rare that they were found in just one individual. In fact, two of these haplotypes comprised over 90% of the total. Lorna has also examined Irish and Gordon Setters: both of these breeds show more variation.

So, English Setters are pretty uniform in their MHC. Does this matter? In humans, there can be problems if two parents are similar in the MHC genetics, with evidence of higher rates of abortion. Whether this occurs in dogs seems not to be known. In humankind, it has been shown that thyroid dysfunction can be associated with particular alleles in Class II MHC, and Lorna's team have evidence that hypothyroidism is associated with the commonest haplotype in English Setters. This is a relatively common condition in the breed and her findings may be very significant to its future well-being. At present, there seems to be little that breeders can do: screening for MHC haplotypes and at present developing breeding plans around this might be a little over the top. However, it is clear that Lorna's research is important for the breed, and should she seek further samples for analysis (especially of dogs known to have hypothyroidism), breeders might remember that offering help can only be in the long-term interests of the breed. Hiding the truth can only damage a breed that is already teetering around the verges of the Kennel Clubs 'endangered' list.

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