Hyperkeratosis in the Irish Terrier – Ongoing research

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Our story started with the Dogue de Bordeaux in 2004, with the French club of the Dogue de Bordeaux (SADB) and the team of Dr Catherine André from the CNRS-University of Rennes.
Then, as the Irish Terriers seem to be affected by a similar disease, we decided to collect also some dogs of this breed, in order to compare both breeds. Few Irish Terriers are present in France but, thanks to a very good contact with a French breeder, we have more contacts in Germany and United Kingdom, where this breed is more popular. The sample collection was really enhanced thanks to some people, particularly Mrs Susan Seabridge in UK and Mrs Andrea Gasch and Helga Richter in Germany, who help us to collect hundreds samples.

1- Clinical description

In humans, inherited palmoplantar keratoderma is a complex heterogeneous group of genodermatoses clinically presenting as hyperkeratosis of the palms and soles. Genetic causes of non syndromic autosomal recessive keratoderma are not well known except for Meleda's disease.

In dogs, footpad hyperkeratosis naturally segregates mainly in two breeds, Dogue de Bordeaux and Irish Terrier. The onset usually occurs in puppies between 10 weeks and 16 months old. Both males and females are affected. A dog without clinical signs after 18 months old is considered healthy.

For the Irish Terrier, clinical signs consist of dermatological lesions affecting footpads showing thickening with severe keratinous proliferations and fissures.

In several affected dogs, troubles of the skin and the hair were observed (ichthyosiform dermatosis). Also, some cases of keratoconjunctivitis sicca were reported. Nonetheless, more clinical information needs to be collected for these skin and eye problems.

2- The collection of samples - inheritance

Currently, we have collected 578 samples of Irish terriers, of which 22 are affected by hyperkeratosis on footpads. Thanks to their pedigree data, we have drawn a very big pedigree of 1100 dogs. The analysis shows an autosomal recessive inheritance.

3- Genetic studies

We performed a genome wide association study on the Illumina array. This array has 170 000 markers, distributed all along the canine genome. Each dog is genotyped for each marker and then, we compare those markers from the

healthy dog against the affected dog to associate some of the markers with the hyperkeratosis.
For this study, we genotyped 13 cases and 21 controls. We observed a genomic region significantly associated with the hyperkeratosis in Irish Terriers. The known genes of this region were studied and one good candidate gene was sequenced. No mutation was found in it.
A complete sequencing of the region of interest was recently done on 4 affected and 4 healthy Irish Terriers. The analyses of these data are on-going.

This research program was a part of the LUPA project financed by the European community until 2012. These funds allowed us to proceed to these genotyping, which are particularly expensive experiments.

4- Next steps

On the genetic side : we are continuing the analysis of the sequence differences observed between affected and healthy dogs.

To understand the physiopathology of the disease, we would need more complete clinical data, particularly regarding the presence of eye or skin disorders in affected and healthy dogs for footpad hyperkeratosis.
For affected dogs, it would be very useful to obtain biopsies of skin and footpad, to do histological examination. Currently, we preserve precious biopsies of 4 Irish Terriers affected by hyperkeratosis. It would be extremely helpful for the research to obtain more biopsies to confirm the first results.
These samples can be done when the dog should be anaesthetized for any other reasons.

We really need samples of affected dogs to advance in the research, and more particularly blood samples (on EDTA tube). Indeed, these blood samples contain more good quality DNA than swab samples.

We warmly thank all the owners, breeders and veterinarians who participate and help us in the collection of samples for the research. The research was funded by Antagene, the CNRS and the European LUPA project (2008-2012).

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Participation to research : what we need

- Blood sample in EDTA tubes (3-5mL)
- Copy of the pedigree
- Sampling certificate (download on our website)
- Clinical data sheet (download on our website)
- Skin and footpad biopsies in Formol and RNAlater (provided by Antagene). These samples can be done when the dog should be anaesthetized for any other reasons.

Antagene, who we are :

Antagene is a biotech company founded in 2002 with the aim of developing genetic tests for the most painful diseases that affect dogs and cats.

As service laboratory, Antagene sells DNA-tests to detect mutation responsible for Cats and Dogs genetic diseases and also genetic identification tests, allowing parentage verifications and pedigree certification of purebred dogs and cats. Currently, Antagene offers more than 50 tests for around 120 different breeds. The team of qualified technicians, engineers and executives, aims of ensuring traceability, quality and responding to customer's needs and expectations.

As a research laboratory, R&D projects are focused on the more severe inherited diseases for animal health and well-being, like ocular, renal, cardiac, or dermatological diseases, in order to develop diagnostic tools for breeders, vets and owners. Our research is mainly collaborative with veterinarians for a clinical diagnostic, and other genetic research teams (Dr Catherine André of the CNRS in Rennes, France…)