Lethal Acrodermatitis in the Bull Terrier – An Update

Lethal Acrodermatitis (LAD) has been described for decades in Bull Terrier dogs in the United States, Canada, Europe and more recently in Australia. Affected dogs present with a highly arched palate in which food gets stuck once the pups begin to eat solid food. The affected puppies are generally smaller than their litter mates and they remain behind in their growth. As they grow older, any of the black patches will change into gray, which is how the breeder often recognizes affected puppies before they show overt signs of disease. The skin on the muzzle and over the footpads becomes crusty and inflamed. The underside of the footpads becomes thickened and eventually the affected puppies will show signs of immune deficiency. Most of the affected puppies also have a hydrocephalus and become increasingly irritated or aggressive. Their quality of life diminishes and most will be humanely euthanized. Earlier studies suggested that this disease is caused by a defect in zinc transport/metabolism but newer studies failed to replicate those results. Because of the results from the older studies, our laboratories have sequenced almost all of the genes currently known to participate in zinc metabolism but we had not found a mutation. Therefore, we performed a genome wide association study (GWAS) to identify the gene(s) involved with this disease, which was made possible by the generous support from the Bull Terrier Club of America and the AKC Canine Health Foundation.

In this case, a GWAS is a method of pairing changes in DNA that are only present in LAD pups but not clinically normal dogs. These changes don't necessarily reflect the mutation but help us marrow down the area in which we have to look for the causal gene and its mutation. One may think of a field with 78 haystacks, with one of them having a needle in it. The GWAS will let you find the haystack that has the needle. Next is the fine mapping, which is equal to finding the needle in the one haystack.

Twenty DNA samples from affected Bull Terriers and 20 from Bull Terriers that were known not to have ever produced affected puppies were used for the GWAS. These samples allowed us to find a region of interest, which we had never expected. Fine mapping efforts have begun and several genes in the region sequenced. We now have received help from Dr. Clare Wade in Australia to expedite the sequencing efforts. We hope to have found the mutation by the end of the year, thus providing the breeders with an accurate DNA based test.

Margret L. Casal, DVM, MS, PhD
Associate Professor of Medical Genetics
School of Veterinary Medicine
University of Pennsylvania.