## Abstract 44:

Recessive deleterious mutations in the TPO gene underlying familial thyroid follicular cell carcinoma in Dutch German longhaired pointers

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Familial thyroid cancer originating from follicular cells accounts for 5-15% of all the thyroid carcinoma cases in humans. Previously, we described thyroid follicular cell carcinomas in a large number of the Dutch German longhaired pointers (GLPs) with likely an autosomal recessive inheritance pattern. Here, we investigated the genetic causes of the disease using a combined approach of genome-wide association study, selective sweep analysis, and ROH analysis based on 170k SNP array genotype data. A region 0-5 Mb on chromosome 17 was identified to be associated with the disease. To locate the potential causal mutations/genes, 22 dogs were sequenced. In the region, two deleterious mutations in the TPO gene; chr17:800788G>A (686F>V) and chr17:805276C>T (845T>M) were identified to be candidate causal mutations. These two SNP were subsequently genotyped in 182 GLPs (54 affected and 128 unaffected) and the recessive genotypes had relative risks of 16.57 and 16.27, respectively. This study provides novel insight into the genetic causes underlying the familial thyroid follicular cell carcinoma and we were able to develop a genetic test to screen susceptible dogs