ABCF MESSENGER

Official Newsletter of the American Boxer Charitable Foundation, Inc.
Virginia Zurflieh, Editor

From the editor: The following update is from Kerstin Lindblad-Toh of the Broad Institute and includes the various boxer health projects on which the Broad and the ABCF, along with many prominent researchers, have collaborated in the past few years. Please pay particular attention to the sections on continuing research into Degenerative Myelopathy and Juvenile Renal Dysplasia.
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Broad Institute Boxer Study Update

Kerstin Lindblad-Toh

Dear boxer folks,

I thought it would be time to give an update on the many projects that the Broad is involved in for the Boxer breed. We have accomplished a lot in the past few years, but there is also quite a bit more work to be done. Here I'll summarize the status of each project:

Degenerative myelopathy:
Together with Drs. Coates and Johnson at the University of Missouri we have identified a mutation in the superoxide dismutase 1 (*SOD1*) gene that confers a major risk to degenerative myelopathy. Mutations in the *SOD1* gene are an underlying cause for some forms of amyotrophic lateral sclerosis (ALS) also known as Lou Gehrig's disease. This discovery has now given us a direction to focus ourselves on the understanding of degenerative myelopathy which will hopefully lead to therapeutic strategies and collaborations with the ALS researchers. While all Boxers who have degenerative myelopathy have two copies (test AT RISK) of this mutation, one cannot be sure that dogs that test AT RISK will get degenerative myelopathy. **In fact the mutation is very common within the breed and breeding away from it at this point, would be dangerous for the breed as a whole.** We did however see some indications that additional genes might be involved in the disease, so we are currently continuing the search for additional loci. This analysis is running on SNP chips right now and we would expect to know more before summer.

While we offer a test and hope to collect as many samples as possible to allow us to find additional risk factors, we would ask that dog owners be patient when submitting samples. This is for two reasons: 1) our sample volume has been tremendously large making it difficult to keep up with the submission process and 2) we believe that **dog owners should not breed according to this test at present** so please have patience with pending test results. Thus, we would like to ask everyone to be considerate of our needs so that we can focus both on the progressing research and getting test
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results back to owners.

Cardiomyopathy:
Together with Dr Meurs at Washington State University we have searched the boxer genome for risk factors for cardiomyopathy. We have found two candidate loci, which we are further examining to find the mutations. We are working closely with Dr. Meurs who is performing the fine mapping and sequencing and we all believe that we are making significant progress. Dr Meurs is planning on giving an update at the National Boxer Show in Ohio in May, so please stay tuned.

Juvenile Renal Dysplasia:
Together with Dr Hedhammar in Uppsala, Sweden, we have searched the genome for genetic risk factors for juvenile renal dysplasia using 12 cases and their parents (or equivalent relatives). Unfortunately we did not find a clear region of association. This might suggest that multiple loci are involved in the disease and that we need more dogs to find these risk factors. Thus, we are now in a phase of renewed samples collection to ensure we get enough samples to identify the disease genes. We currently have over 20 cases collected, but need at least 50 to perform the next genome-wide screen. We have been getting a good response in the US and in Sweden, but still really need more affected dogs from the US.

Hemangiosarcoma:
In collaboration with Dr Azuma at Tufts University we have performed a SNP scan and found six candidate regions in the Golden retriever that appear to confer a risk to hemangiosarcoma. Further study of these regions suggests that one of these regions may be a risk factor also in the boxer breed, although analysis with more boxer dogs may potentially suggest association at more loci. We are currently looking for the actual mutations at these loci. We would very much like to receive more samples from boxers with hemangiosarcoma. We are also looking for tumor tissue to study the effect of potential mutations on the nearby genes. If you are able to submit tissue in addition to a blood sample please contact dog-info@broad.mit.edu prior to taking the sample.

Osteosarcoma:
Together with Dr Comstock at University of Michigan we have performed SNP scans in both the Rottweiler and Greyhound breeds and found three potential loci in each breed. Follow-up analysis of these regions has been done in multiple breeds and is currently ongoing in the boxer breed. We are also in the process of searching for the actual mutations. Again tissue samples would be of real value for follow-up work.

Mast cell tumors:
In collaboration with Dr London we have identified have identified four candidate regions by SNP scanning the Golden Retriever breed. None of these appear to be present in the boxers. However, we have already collected over 30 cases, so if we continue to collect samples, we could very

	well envision a separate genome scan in the boxer breed. **Lymphoma:** Together with Matthew Breen, we have just performed a preliminary B cell lymphoma scan in golden retrievers and are finding at least one plausible candidate locus. We expect to include boxers in the fine-mapping stage shortly. **In conclusion,** I hope that you are as excited as we are about the progress we are making. We also ask you to keep in mind that when performing any of these studies it is critical for us to have the most updated status for all dogs. We therefore request owners who have previously submitted samples to us to contact us if the health status of their dogs changes in any way. Kind regards, Kerstin Lindblad-Toh Scientific Director, Vertebrate Genome Biology Broad Institute of MIT and Harvard Professor, Uppsala University, Sweden