ISAG Conference 2008, Amsterdam, The Netherlands

Dog Genome Mapping Workshop

Chair**: Kathryn T. Graves**, University of Kentucky, USA.

Around 60 people attended the workshop.

The workshop was called to order at 15:30 by Chair Kathryn Graves. Committee member Alan Wilton was present, committee members Mathew Binns and Cathryn Mellersh were not in attendance at the conference.

A sign-in sheet was circulated for attendees to sign and supply their email addresses. A total of 57 people were in attendance.

The Chair introduced the key speaker, Dr. Leif Andersson of the University of Uppsala, Sweden. Dr. Andersson's talk was entitled "Genome-Wide Association Analysis: A Powerful Method for Finding Genes Underlying Phenotypic Diversity in the Dog."

Dr. Andersson started by offering the dog as a model for many human diseases, but because of the more extensive linkage disequilibrium in the dog, studies could be successfully conducted with smaller sets of affected and control dogs with fewer SNPs (15k vs 500k) than needed in human studies. For a recessive trait as few as 20 affecteds and 20 controls were sufficient; for a dominant trait the number increases to 50 + 50. A complex trait could require at least 100 + 100.

He used the example of his group's success in elucidating the white spotting locus (S locus) in the Boxer. Genome-wide SNP analysis within the Boxer breed revealed a strong correlation with the *MITF* (microphthalmia-associated transcription factor) locus. Mutations exist in this gene in other species that affect melanocyte migration and survival. Fine mapping across breeds localized the mutation to a ~100bp region within the MITF gene.

He described other success stories such as identifying the mutation responsible for the ridge in Rhodesian Ridgebacks due to duplication of fibroblast growth factor genes.

Ongoing projects were also presented, such as a couple of complex conditions in the Nova Scotia Duck Tolling Retriever-immune-mediated arthritis and steroid-responsive meningitis.

He also brought to the audience's attention the LUPA Initiative, started in 2008, which is a wide scale European project to use the dog as a model for human disease.

After answering numerous questions, Dr. Andersson was again thanked and the shorter poster presentations began. First to speak was Dr. Alan Wilton, University of New South Wales, Australia, who spoke on poster 2178 entitled "Disease Identification in Dogs: Use of SNP Arrays and Candidate Genes". He compared the candidate gene approach to the use of SNP array technology to identify the mutation responsible for disease. He used Trapped Neutrophil Syndrome in Border Collies as an example of candidate gene approach and cerebellar abiotrophy in kelpies as an example of Genome Wide Analysis with SNP arrays. He illustrated that although Affy SNP chips exist with huge numbers of SNPs , over half are not unreliable on the current V2 array, which can cause difficulties in analysis.

One additional project he mentioned is to identify a panel of SNPS that can verify the purity of animals that are purportly Dingos.

The next poster presentation was by Dr. Barbara Zangerl of the University of Pennsylvania School of Veterinary Medicine on poster 2130 "CFA9 Association Study to Identify Progressive Rod-Cone Degeneration in the Dog. Dr. Zangerl introduced her topic by saying that PRCD was first recognized in Cocker Spaniels and Miniature and Toy Poodles over 40 years ago. It is now known that PRCD affects at least 27 breeds. Although it is autosomal recessive, it has different rates of progression. Different breeds have the same mutation but a different rate of progression designated "fast" and "slow". Her study used the Affymetrix SNP chip containing 4962 CFA9 SNPs, however only 1807 of these gave useable results. A strong signal was obtained at the mutation site, but another strong peak area was also identified that she explained could point to a modifier locus. A potential candidate gene in this region is ACCN1. She cautioned that there is a large failure rate or false heterozygote rate on the large SNP chips and many of the analysis programs are created for use with the human genome.

The final presentation was given by Dr. Cord Drogeműller from the University of Berne, Switzerland on poster 2193 "Positional Cloning of the Canine Hairless Mutation reveals an Essential Role for the *FOXi3* Gene in Ectodermal Development". Canine ectodermal dysplasia refers to a condition in which the dogs have a hairless pattern and abnormal tooth development. It is an autosomal semi-dominant trait mapped to CFA17 by LD and it is lethal

in the homozygous form. The Chinese Crested, Mexican Hairless and Peruvian Hairless are examples of breeds exhibiting the hairless phenotype. The 20+20 scheme discussed by Dr. Andersson earlier was used. And a SNP on CFA17 was identified. A genome-wide haplotype association was done and all hairless dogs had one copy of an 8 SNP 160kb haplotype. *FOXi3* was identified as a candidate gene in this region and exons 1 and 2 were sequenced with some challenges due to high GC content in the hairless dogs. All 140 hairless dogs were heterozygous for a 7 bp duplication while none of the 55 coated dogs from the breeds studied had the duplication. Since studies in mouse embryos showed *Foxi3* transcript in the developing teeth and whisker placodes, it was concluded that this mutation is the causative mutation for the hairless phenotype in dogs.

After the presentations, the election for the new standing committee was held. The new committee members unanimously voted in are: Alan Wilton (Chair), Kathryn Graves, Cathryn Mellersh, Matthew Binns and Cord Drőgeműller. Dr. Wilton was provided with the list of attendees.

Discussion among committee members has decided to name the Workshop the Dog Genome Workshop in future as it will include other activities besides mapping.