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The use of genomic data for the analysis of companion animals

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Domestic dogs

- selection pressure of the breeders → huge phenotypic variability between breeds

- era of modern breeding
  - low haplotype diversity and extensive linkage disequilibrium
  - substantial reduction of genetic diversity within certain lineages
  - purebred dogs – 20 % autozygosity

- genome-wide canine SNP arrays
  - phylogeny, paternity
  - genetic diversity within and between breeds
  - genetic structure of population and level of admixture
  - genomic inbreeding
  - effective population size
  - mapping disease loci

Objectives

- to identify excessively homozygous regions in three different breeds of dogs:
  the Golden, Labrador and Nova Scotia Duck Tolling Retriever
- to examine level of admixture among breeds

Material & Methods

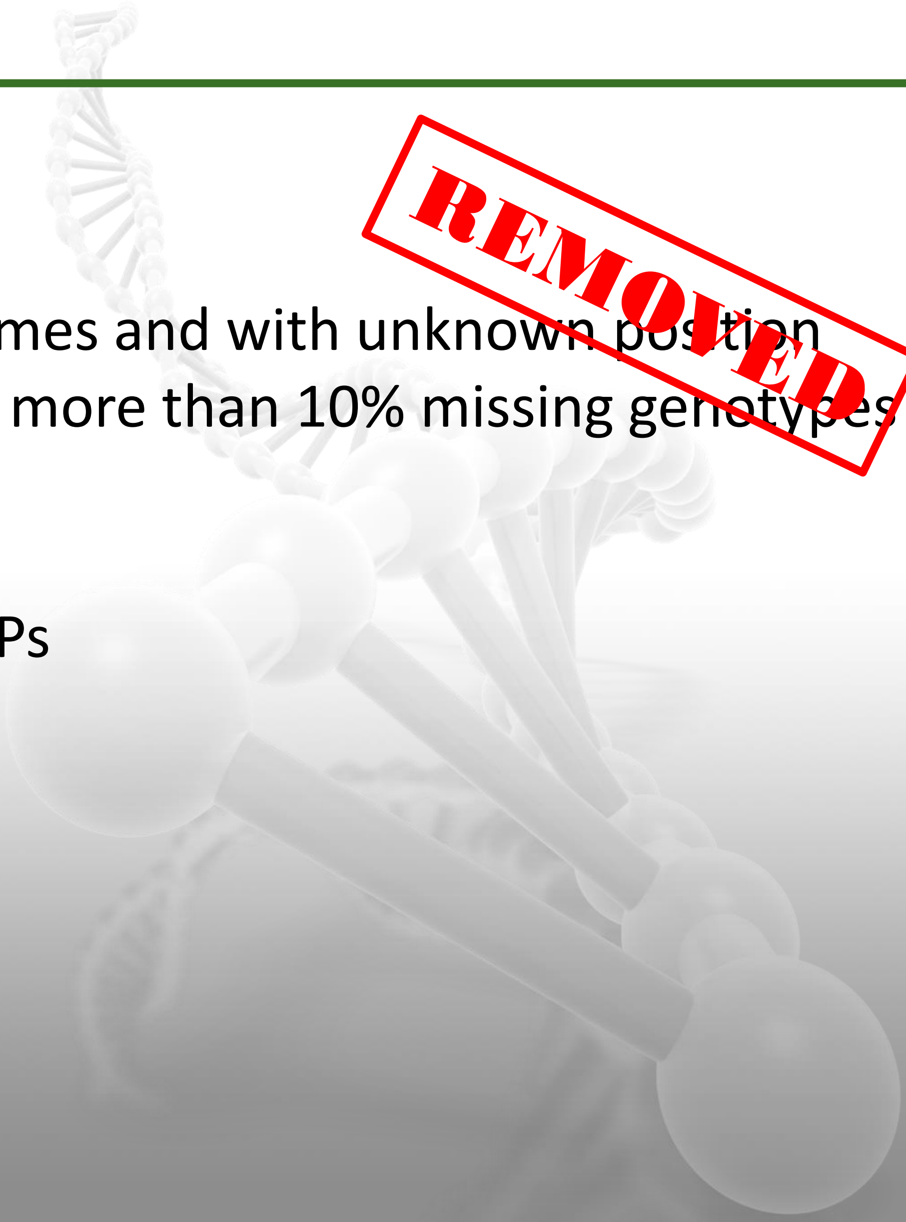
Analysed population – overall 51 dogs

- 14 Golden Retrievers (GRe)
- 14 Labrador Retrievers (LRe)
- 23 Nova Scotia Duck Tolling Retrievers (NSD)

Whole genome Illumina CanineHD Whole-Genome Genotyping BeadChip (publicly available dataset from the LUPA project; Vayssem et al., 2011)

Vayssem, A., Ratnakumar, A., Derrien, T. et al. 2011. Identification of genomic regions associated with phenotypic variation between dog breeds using selection mapping. PLoS Genetics, 7, e1002316.

Material & Methods



Quality control

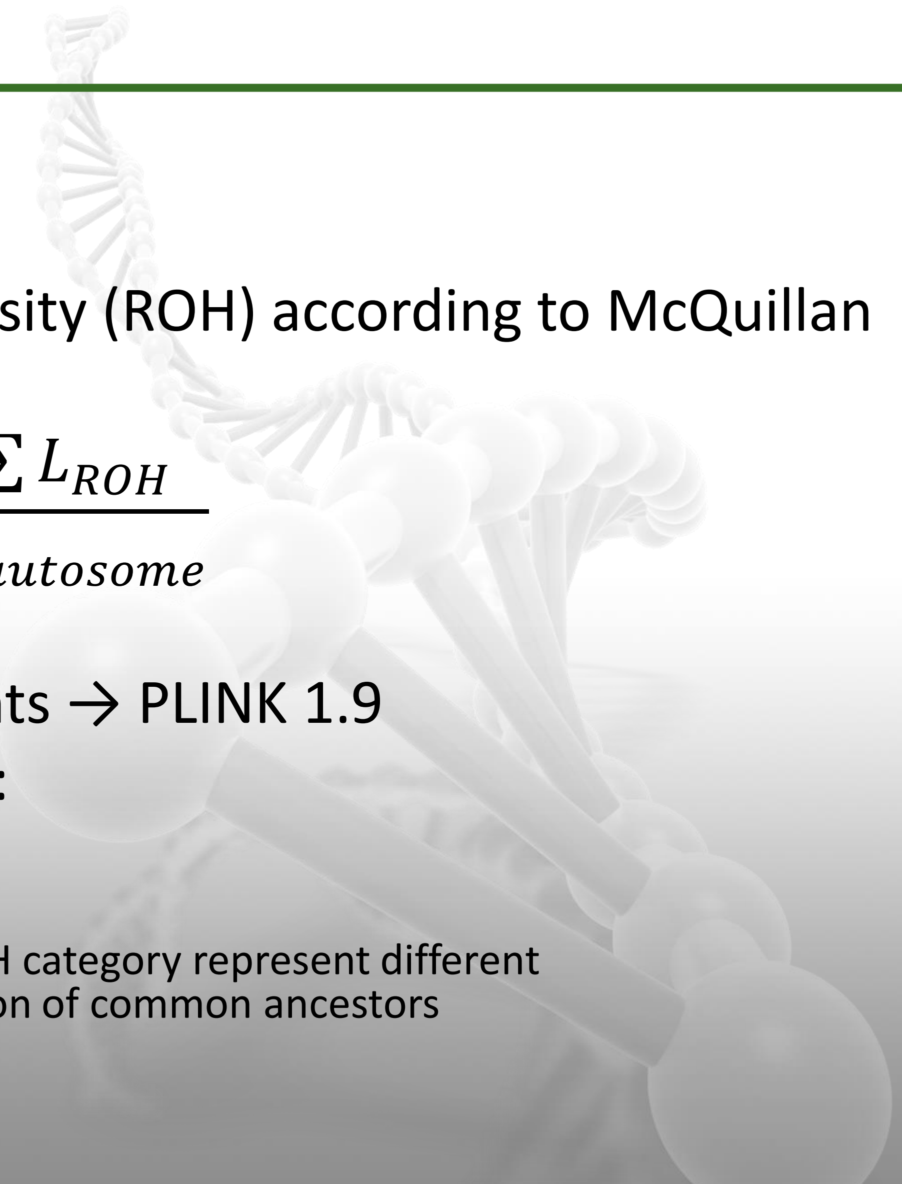
- PLINK 1.9
    1. SNPs on sex chromosomes and with unknown position
    2. animals and SNPs with more than 10% missing genotypes

REMOVED

Final Database: 51 animals

173,662 SNPs

Material & Methods



Genomic inbreeding (F_{ROH})

- Based on runs of homozygosity (ROH) according to McQuillan et al. (2008):

$$F_{ROH} = \frac{\sum L_{ROH}}{L_{autosome}}$$

- Distribution of ROH segments → PLINK 1.9
- Five inbreeding coefficients:
    - F_{ROH}>1Mb
    - F_{ROH}>2Mb
    - F_{ROH}>4Mb
    - F_{ROH}>8Mb
    - F_{ROH}>16Mb

each ROH category represent different generation of common ancestors

McQuillan R., Leutenegger A., Abdel-Rahman R., Franklin C., Pericic M., Barac-Lauc L., Smolej-Narancic N., Janicijevic B., Polasek O., Tenesa A., Macleod A., Farrington S., Rudan P., Hayward C., Vitart V., Rudan I., Wild S., Dunlop M., Wright A., Campbell H., Wilson J. (2008). Runs of homozygosity in European populations, Am J Hum Genet , Vol. 83, pp. 359-372.

Material & Methods

Genetic structure & level od admixture

- Bayesian clustering method – BAPS (Corander et al., 2004)

  posterior mode estimates of the admixture coefficients

- network-visualization - NetView (Steinig et al., 2016)

Corander, J., Waldmann, P., Marttinen, P., Sillanpä, M.J. 2004. BAPS 2: enhanced possibilities for the analysis of genetic population structure. Bioinformatics, 20: 2363-2369.

Steinig, E.J., Neuditschko, M., Khatkar, M.S., Raadsma, H.W& Zenger, K.R. 2016. NETVIEW P: a network visualization tool to unravel complex population structure using genome-wide SNPs. Mol Ecol Resour. 16: 216-227.

Results I.

ROH segments in the dog genomes

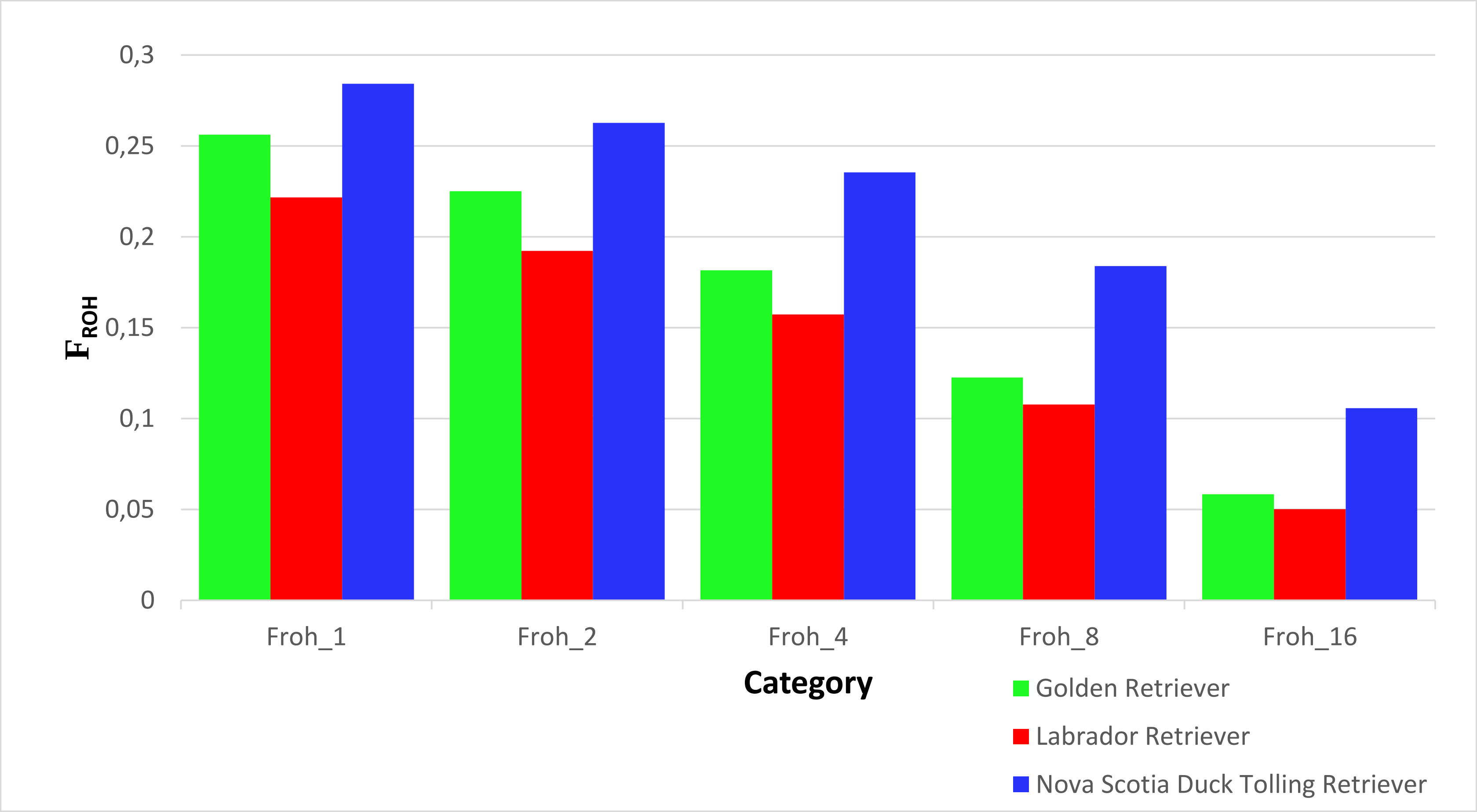
The total segments length (in Mb) and number (in brackets) of runs of homozygosity (ROH) with different size (>1, 2, 4, 8, and 16 Mb)

	GRe	LRe	NSD
Total length (Number)	Mean ± SD		
ROH >1 Mb	553.61 ± 211.56 (122.64 ± 28.05)	479.11 ± 122.15 (107.64 ± 17.71)	614.16 ± 110.99 (97.39 ± 12.28)
ROH >2 Mb	486.51 ± 206.91 (74.36 ± 21.53)	415.63 ± 117.43 (61.43 ± 12.75)	567.91 ± 111.78 (64.21 ± 9.27)
ROH >4 Mb	392.59 ± 195.07 (40.64 ± 14.52)	339.85 ± 113.57 (34.93 ± 10.08)	509.07 ± 118.40 (43.57 ± 9.29)
ROH >8 Mb	264.97 ± 175.5 (17.57 ± 9.23)	232.99 ± 94.01 (16.00 ± 5.45)	397.54 ± 113.26 (24.04 ± 6.68)
ROH >16 Mb	126.20 ± 139.08 (5.21 ± 4.81)	108.53 ± 71.97 (4.64 ± 3.08)	228.46 ± 77.61 (8.70 ± 2.65)

Golden (GRe), Labrador (LRe) and Nova Scotia Duck Tolling (NSD) Retrievers

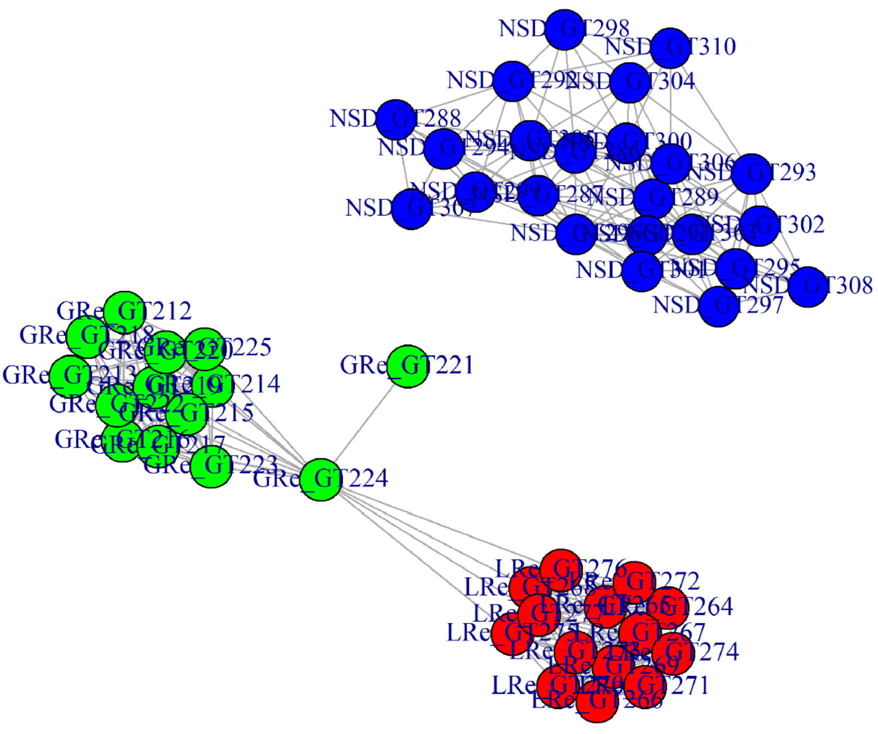
Results II.

Genomic inbreeding (F_{ROH})



Results III.

Population structure

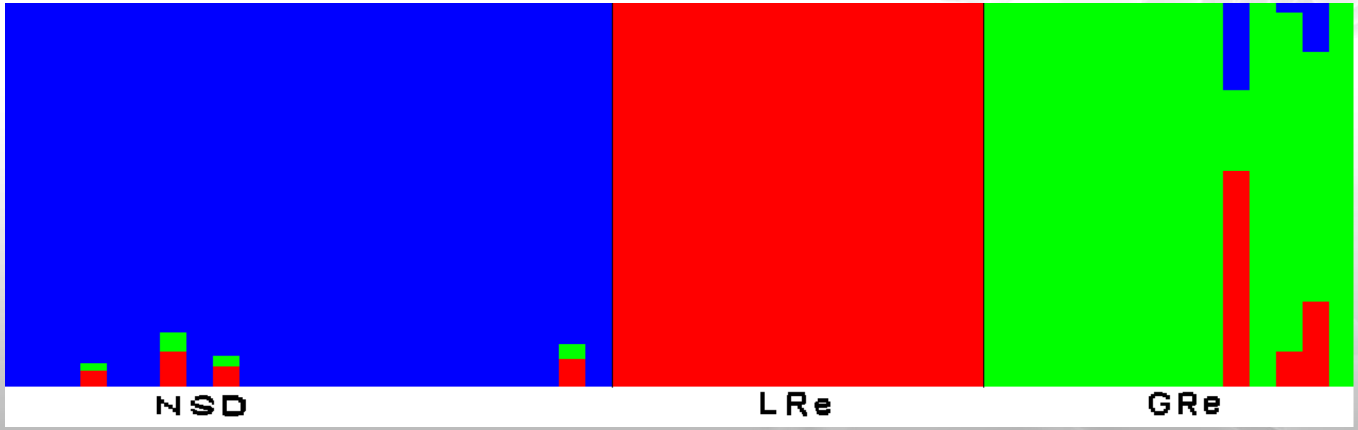


Metapopulation of Nova Scotia Duck Tolling Retriever (NSD – blue), Labrador Retriever (LRe – red) and Golden Retriever (GRe – green) visualized by network approach

Results IV.

Level of admixture

Cluster membership suggested by the “unsupervised” BAPS algorithm



Nova Scotia Duck Tolling Retriever (NSD) in blue, Labrador Retriever (LRe) in red and Golden Retriever (GRe) in green

Conclusion

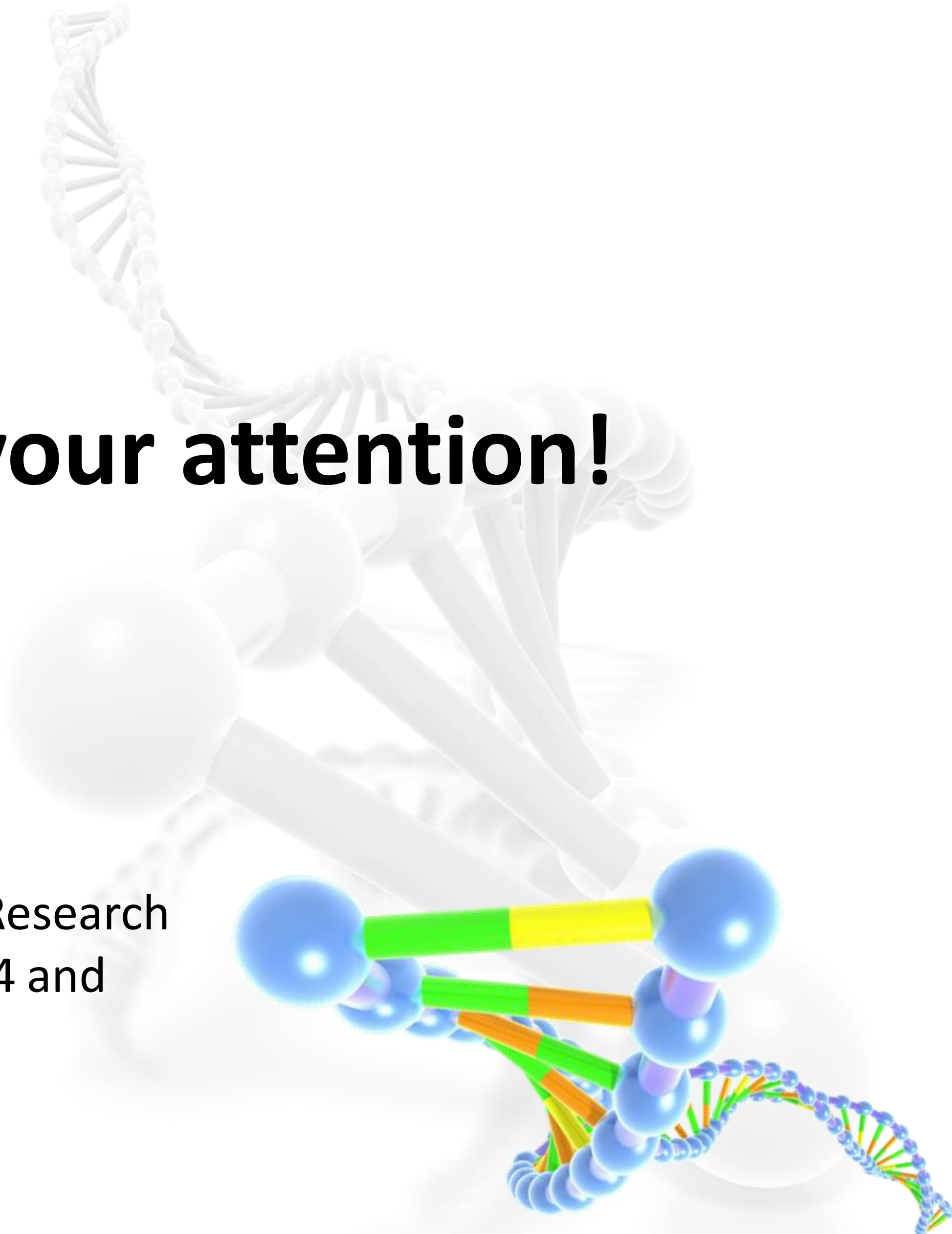
- Distribution of ROH segments >1 MB confirmed expected proportion of autozygosity (~20 %) across dog genome
    - 25.62 % Golden Retriever
    - 22.17 % Labrador Retriever
    - 28.41 %Nova Scotia Duck Tolling Retriever
- Inbreeding estimated by ROH >16 reached 5.02% (LRe) - 10.57% (NSD)
- Analysed breeds ⟶ genetically connected with extremely high level of recent as well as historical inbreeding
- Between breeds → relatively low level of genetic admixture

Conclusion

Future analysis of identified ROH ......

- explanation of evolutionary changes which shaped the genome due to natural as well as artificial selection → selection signatures
- identification of domestication-related loci, loci associated with desired phenotype condition or diseases
- analysis of unique genomic region in case of genetically very close local populations

Thank you for your attention!



Acknowledgement

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