Genomic variability among cattle populations based on runs of homozygosity

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GENOMIC VARIABILITY AMONG CATTLE POPULATIONS BASED ON RUNS OF HOMOZYGOSITY

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SUMMARY

In this work, the distribution of different lengths ROH (runs of homozygosity) in six cattle breeds was described. A total of 122 animals from six cattle breeds (Holstein, Simmental, Austrian Pinzgau, Ayrshire, MRI-Meuse Rhine Issel and Slovak Pinzgau) were analysed. The ROH approach was used to distinguish Slovak Pinzgau population from other investigated breeds as well as to differentiate between ancient and recent inbreeding. The average number of ROH per animal ranged from 17.06 in Holstein to 159.22 in Ayrshire. The highest number of short ROH (ancient inbreeding) was found in Simmental, followed by Ayrshire. The Ayrshire and MRI had a higher proportion of longer ROH distributed across the whole genome, revealing recent inbreeding. ROH were identified and used to estimate molecular inbreeding coefficients (F_{ROH}). The highest level of inbreeding from the investigated breeds was found out in Ayrshire with the same tendency for all length categories compared to Slovak Pinzgau with higher ancient inbreeding. Ancient inbreeding was only observed in Holstein population. A similar trend is becoming apparent even for Slovak Pinzgau, showing the second smallest recent inbreeding. Therefore, it is necessary to preserve the given population in the original phenotype and prevent further increase of inbreeding especially in endangered breeds.

Key-words: autozygosity, diversity, genotyping array

INTRODUCTION

High throughput genotyping allows a new and more accurate view on rates and effects of inbreeding in livestock (Ferenčaković et al., 2013a, Purfield et al., 2012). Long stretches of homozygous genome that most likely arise when the individual is the offspring of related individuals represent ROH (runs of homozygosity). When related individuals mate, the offspring carry long sections of the genome that are homozygous and identical by descent (IBD). Long ROH are most likely derived from a recent ancestor; shorter ones, from a more distant one. Long ROH thus correspond to recent inbreeding, whereas shorter ROH indicate more distant ancestral effects (ancient inbreeding) such as breed founder effects (Purfield et al. 2012). Calculating how much an individual's genome occurs as ROH of particular lengths provides information about levels of inbreeding relative to reference populations specific numbers of generations ago (Curik et al., 2014). Another advantage of inbreeding estimation based on genomic information is related to the fact that it is possible to differentiate local vs. genome-wide effect of inbreeding. For instance, Purfield et al. (2012) identified several genomic regions with particularly large ROH inbreeding in cattle, those regions potentially containing genes associated with traits of interest (immunity, carcass, dystocia).

Slovak Pinzgau is a traditional dual purpose breed, introduced approximately 150 years ago (Kasarda et al., 2014). Thanks to its unique traits as longevity, fertility, health, grazing ability it had been bred in mountainous areas of northern Slovakia (Pavlík et al., 2014). Due to significant decline of the population in last decades this breed is considered endangered (Kadlečík et al., 2008). From the beginning, only purebred animals were used for breeding. Approximately 60 years ago, the breed was started grading-up with other breeds in order to increase milk production while unique dual-purpose character was preserved. Jersey breed was

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used rather experimentally whereas Ayrshire, Meuse Rhine Issel (MRI), Red Holstein have been successfully proved and Red Holstein has been used up to this day. Nowadays, sires used originated mostly from Slovakia and some from Austria, due to a small number of sires, but pedigrees are generally connected. Austrian Pinzgau has been bred with Red Holstein and Simmental until the second half of the last century (Pšenica, 1990).

Since Pinzgau belongs to autochthonous breeds of Slovakia, clear distinction from other populations is necessary. There are many known methods based on genomic data as principal component analysis, F_{ST} values, genetic distances, structure analysis, admixture analysis. The aim of this study was to evaluate general ROH analysis for Slovak Pinzgau cattle and five related breeds.

MATERIAL AND METHODS

The population of sires of Pinzgau cattle from Slovakia were analysed. Genomic DNA for each of 19 semen samples was genotyped at a commercial lab using the Illumina BovineSNP50 v2 BeadChip. The genotyping array contained 54,609 SNPs. To understand the genetic relationship within and among breeds, genotypes from 103 other animals belonging to 5 domesticated bovine breeds (Holstein-54, Simmental-23, Austrian Pinzgau-5, Ayrshire-18 and MRI-3) were obtained from Decker et al. (2014a) and Gautier et al. (2010a). Despite the fact that Decker et al. (2014b) and Gautier et al. (2010b) removed closely related individuals from the dataset if pedigree data were available, current numbers of Slovak Pinzgau cattle did not allow us to perform the same exclusion. Due to use of more data sets new genetic map was created. In order to minimize risk of genotype errors and excluding poorly performing SNPs individual quality control was performed. Excluded were

animals with more than 5% and SNP markers with more than 10% of missing genotypes by PLINK (Purcell et al., 2007). Minor allele frequency was not used as an exclusion criterion in this analysis, so that the detection of homozygous segments was not compromised. Further analyses were performed including information from 42 852 autosomal SNPs common to all breeds.

In this study, the minimum length of ROH was set at 1 Mb on the basis of the theoretical relationship between distribution of IBD fragments and the number of generations since a common ancestor. ROH were placed into five groups following approach of Ferenčaković et al. (2013a), identified as ROH > 1Mb , ROH > 2Mb , ROH > 4Mb , ROH > 8Mb and ROH > 16 Mb. For each individual in each of the six breeds, and for each ROH length category the total number of ROH detected, the average length of ROH (in Mb) and the sum of all ROH segments by animals (in Mb) were calculated. The inbreeding coefficient based on ROH (F_{ROH}) was defined as the length of all ROH in the genome divided by specified length of the autosomal genome covered by SNP according to McQuillan et al. (2008). The level of F_{ROH} in different length categories was determined to differentiate between ancient and recent inbreeding. The difference among individual breeds based on total length and total number of ROH was confirmed using F-test.

RESULTS AND DISCUSSION

Total length and number of determined ROH > 1 Mb per each of 122 individual is shown in Figure 1. Total number and length of ROH differed significantly (p<0.0001) among populations which historically contributed to the Slovak Pinzgau origin. The highest mean number of ROH was found in Ayrshire (159.22), followed by Simmental (143.78).
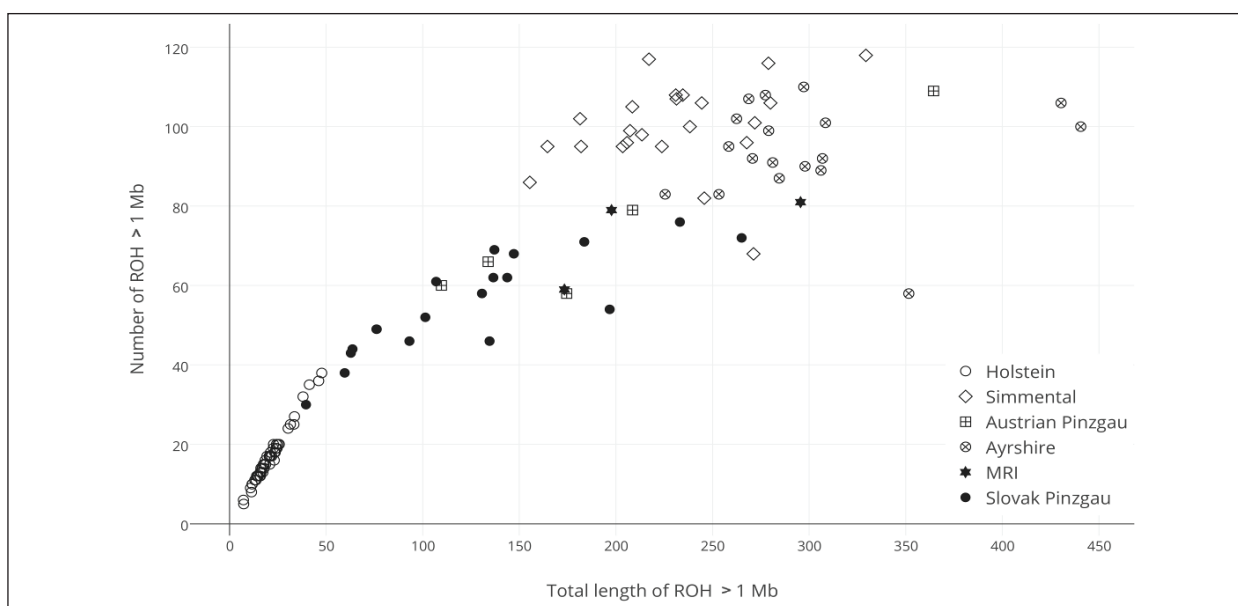

Figure 1. Relationship between number and total length of ROH (run of homozygosity) in 122 animals belonging to 6 breeds examined

The inbreeding coefficient derived from ROH in different length categories was used to differentiate more evident between ancient and recent inbreeding. The average number of the shortest ROH (related to ancient kinship) per animal ranged from 16.89 ± 6.92 in Holstein to 99.96 ± 11.34 in Simmental, similarly to the results of Austrian Simmental obtained by Ferenčaković et al. (2011). The Ayrshire and MRI had a higher proportion of longer ROH distributed across the whole genome, revealing recent inbreeding. Present livestock populations consist of a large number of cows decreasing number of sires and intensive selection for dairy production leading to a reduction of effective population size and increase of inbreeding. Planned mating strategy has been used in order to avoid the problem. Otherwise, only ancient inbreeding was observed in Holstein population (Figure 2).

The similar trend has been becoming apparent even for Slovak Pinzgau considered as dual-purpose cattle as well as for Simmental in study of Marras et al. (2015), whilst Purfield et al. (2012) noticed the highest recent inbreeding in Holstein. Differences in the F_{ROH} depend on selected animals and chosen length categories for ROH computation. The same tendency for all length categories was examined in Ayrshire with the highest values of inbreeding coefficient from all the investigated breeds. Mainly ancient inbreeding in Slovak Pinzgau was found out. The genomic inbreeding coefficients ranged from 0.0212 ± 0.0216 to 0.1206 ± 0.0226 in Ayrshire while from 0.0055 ± 0.0074 to 0.0505 ± 0.0245 in Pinzgau for $F_{ROH > 16\,Mb}$ and for $F_{ROH > 1\,Mb}$, respectively. The overall mean values of F_{ROH} across all length categories were 0.017 ± 0.0037 in Holstein, 0.0411 ± 0.0341 in Simmental, 0.0409 ± 0.0368 in Austrian Pinzgau, 0.0683 ± 0.0425 in Ayrshire, 0.0496 ± 0.0333 in MRI, and 0.0238 ± 0.0244 in Slovak Pinzgau. Thus, F_{ROH} differed significantly among breeds. The F_{ROH} values examined by Ferenčaković et al. (2013b) for all length categories in Austrian Pinzgau bulls were in between those obtained in the present study for Slovak and Austrian Pinzgau.
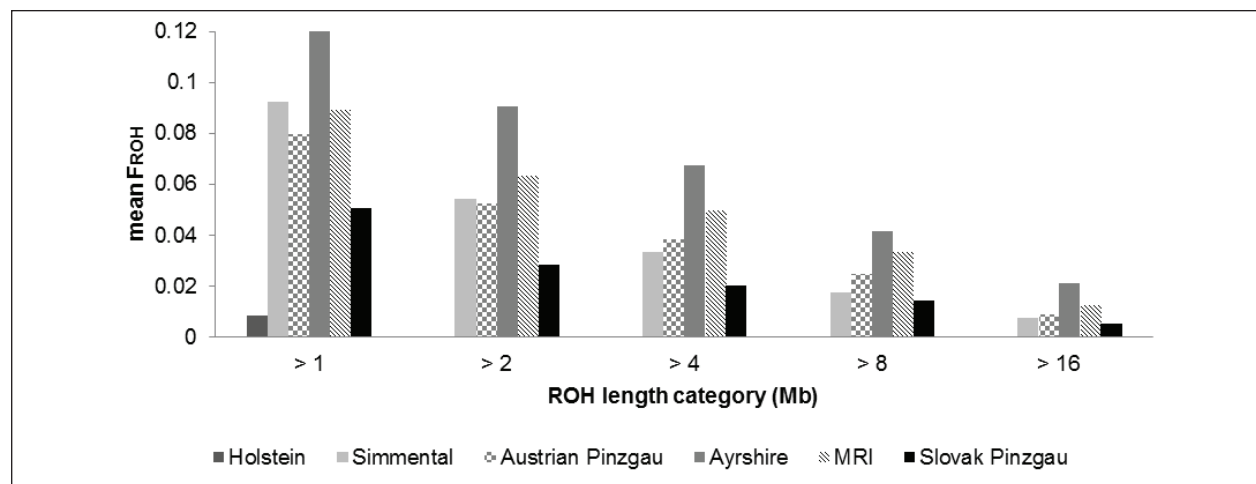

Figure 2. Inbreeding coefficient computed for different length categories ($F_{ROH > 1, > 2, > 4, > 8}$ and $_{> 16\,Mb}$) in six breeds investigated

CONCLUSION

Total number of ROH and total length of ROH have shown genomic differences of the populations historically contributing to Slovak Pinzgau. The study provides results about the inbreeding independent of pedigree information. Historical formation of the breeds as well as present mating strategies within the breeds should be taken in the account for detection ancient or recent inbreeding. The absence of recent inbreeding in Holstein could be caused by selection of individuals for the performed analyses. Higher ancient inbreeding was obtained in Slovak Pinzgau, taking into account only this population. In comparison with other breeds showing the second smallest recent inbreeding it is necessary to preserve the given population in original phenotype. Regular monitoring of genetic diversity including inbreeding trends is necessary as this information is needed in population management.

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