RESEARCH ARTICLE

Genome-wide association study reveals candidate genes relevant to body weight in female turkeys (*Meleagris gallopavo*)

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Abstract

The underlying genetic mechanisms affecting turkey growth traits have not been widely investigated. Genome-wide association studies (GWAS) is a powerful approach to identify candidate regions associated with complex phenotypes and diseases in livestock. In the present study, we performed GWAS to identify regions associated with 18-week body weight in a turkey population. The data included body weight observations for 24,989 female turkeys genotyped based on a 65K SNP panel. The analysis was carried out using a univariate mixed linear model with hatch-week-year and the 2 top principal components fitted as fixed effects and the accumulated polygenic effect of all markers captured by the genomic relationship matrix as random. Thirty-three significant markers were observed on 1, 2, 3, 4, 7 and 12 chromosomes, while 26 showed strong linkage disequilibrium extending up to 410 kb. These significant markers were mapped to 37 genes, of which 13 were novel. Interestingly, many of the investigated genes are known to be involved in growth and body weight. For instance, genes AKR1D1, PARP12, BOC, NCOA1, ADCY3 and CHCHD7 regulate growth, body weight, metabolism, digestion, bile acid biosynthetic and development of muscle cells. In summary, the results of our study revealed novel candidate genomic regions and candidate genes that could be managed within a turkey breeding program and adapted in fine mapping of quantitative trait loci to enhance genetic improvement in this species.

Introduction

Turkeys are mainly raised for meat and turkey production has increased worldwide in the last few years with the global market for turkey meat increasing to approximately 6 million tonnes per year between 2016 and 2019 [1]. Producing rapidly growing turkeys has been motivating breeders and farmers in response to the global high demand for meat [2, 3]. Thus, improving growth and yield are central to the turkey breeding objectives aimed at increasing production and minimizing costs [4–6]. Studies have shown high positive genetic correlations between
Genetic parameters revealed that selection may not favour all traits of interest [6, 9, 10]. In this context, genome-wide association studies (GWAS) have been widely used to better understand the genetic architecture of complex traits through the identification of quantitative trait loci (QTL) harboring candidate loci.

QTLs affecting body weight have been previously reported in chickens (e.g. [11–13]), pigs [14] and beef [15]. For turkeys, despite several QTLs detected based on QTL mapping [4], no GWAS investigations have been performed to assess body weight. QTL mapping has been useful for detecting QTLs with relatively large effects, however, it does lack power in accurately modeling QTL with small effect, especially for complex traits such as body weight [16]. The current available high-density turkey genomic data opens the door to conduct GWAS, which may boost breeding programs in this species and overcome the unfavorable genetic correlations between traits of interest such as body weight and walking ability [5]. The objective of this study was to identify genetic variants and candidate genes associated with 18-week body weight (BW) in turkeys using GWAS in a turkey population genotyped with a proprietary 65K SNP array.

Materials and methods

Ethics statement

This study was carried out in accordance with the principles of the Canadian Council on Animal Care, the Hendrix Genetics Animal Welfare Policy, and the University of Guelph Animal Care Committee. The protocol was approved by the University of Guelph Animal Care Committee (Animal Use Protocol #3782).

Study population

Phenotypic and genomic data for 24,989 female turkeys from a male line were provided by Hybrid Turkeys, Kitchener, Canada. The birds hatched between 2010 and 2019 and were reared under a standard feeding system with group housing and shared feeders and drinkers. At 18 weeks of age, bodyweight was recorded with an average of 12.91 ± 0.87 kg. Blood samples were collected from each bird to extract DNA using standard industry procedures, and animals were genotyped using a proprietary 65K single nucleotide polymorphism (SNP) array (65,000 SNP; Illumina, Inc.). Markers in non-autosomal regions were removed and missing SNPs were imputed for missing SNPs using Beagle 5.1 [17]. Quality control for the imputed data was performed using PLINK software [18], where SNPs were removed if they had a minor allele frequency lower than 0.05 or significantly deviated from Hardy Weinberg proportions ($P < 1 \times 10^{-8}$). The number of markers retained for subsequent analyses was 48,715.

More details about this data are presented in Abdalla et al. [5, 19].

Statistical analyses

Prior to GWAS, principal component (PC) analysis was implemented in PLINK [18]. Using the indep-pairwise option in PLINK, SNP markers were pruned with a window size of 25 markers, a step of 5 markers, and a $r^2$ threshold of 0.2. This procedure resulted in 3,891 independent markers which were used to derive the top two PCs. To evaluate the association
between SNPs and BW, the following univariate linear mixed was fitted

\[ y = W\alpha + x\beta + u + e, \]

where \( y \) is an \( n \times 1 \) vector of phenotypic values for \( n \) individuals, \( W \) is an \( n \times c \) matrix of covariates (fixed effects) that control the population structure (top 2 PCs) and hatch week-year, \( \alpha \) is a \( c \times 1 \) vector of the corresponding coefficients, \( x \) is an \( n \times 1 \) vector of marker genotypes at the locus being tested, \( \beta \) is the effect size of the marker, \( u \) is an \( n \times 1 \) vector of random polygenic effects with a covariance structure as \( u \sim N(0, K\sigma_g^2) \), where \( K \) is the genetic relationship matrix derived from SNP markers and \( \sigma_g^2 \) is the polygenic additive variance, and \( e \) is an \( n \times 1 \) vector of random residuals with \( e \sim N(0, I\sigma_e^2) \), where \( I \) is an \( n \times n \) identity matrix, and \( \sigma_e^2 \) is the residual variance component.

Population stratification was assessed using a quantile-quantile (Q–Q) plot in addition to an inflation factor (\( \lambda \); Yang et al. [20]), which was calculated by dividing the observed median value of the Chi-squared statistic for p-values (obtained from GWAS) by the expected median value of the Chi-squared statistic (approximately 0.456 for 1 df tests). Significant SNPs were determined using a genome-wide false discovery rate (FDR) of 5% [21]. This approach was chosen as it provides a higher power while controlling false discovery rate. The negative logarithm of the P-value for each SNP was displayed in a Manhattan plot and a genome wide line for the 5% FDR was drawn to display significant SNPs. Q–Q and Manhattan plots were generated using qqPlot and Manhattan functions, respectively, available in R [22]. Heritability of BW and phenotypic variance explained by the significant SNPs associated with BW was estimated by fitting a linear model using restricted maximum likelihood implemented in GCTA software [23]. To characterize candidate regions that affect bodyweight, linkage disequilibrium (LD) analysis was performed for the chromosomal regions with multiple clustered significant SNPs using PLINK software [18].

**Assignment of significant SNPs to genes**

The Turkey 5.1 assembly [24] was used to assign significant SNPs to genes. In chickens, strong linkage disequilibrium (LD) has been reported to extend up to 10–150 kb [25–27]. In this study, SNPs were assigned to genes if they were located within the genomic sequence of an annotated gene or within 15 kb of the 5’ or 3’ ends of the first and last exons, respectively. This distance is expected to capture proximal regulatory regions and other functional sites that may lie outside but close to the gene such as promoter regions.

**Results and discussion**

Deviations from the identity line to the left of the Q–Q plot suggest strong association of BW with the SNPs as shown in Fig 1. The genomic inflation factor was 0.84 indicating the absence of population stratification, therefore no adjustment was necessary [28, 29]. Q–Q plots were also obtained after removing the significant SNPs as well as without adjustment for the population stratification. These plots are presented in the supplementary material (S1 and S2 Figs). Based on an FDR of 5%, the Manhattan plot in Fig 2 shows the 33 SNPs that were significantly associated with BW in turkeys and these are shown in Table 1. Among these significant SNPs, 8, 2, 2, 4, 5 and 12 were located on *Meleagris gallopavo* autosomal chromosomes (MGA) 1, 2, 3, 4, 7 and 12, respectively. The minor allele frequency for the significant SNPs ranged between 0.10 and 0.47 and their effect on BW ranged between -0.15kg ± 0.01 and 0.12kg ± 0.03. Heritability of BW was 0.52 ± 0.01 and the phenotypic variance explained by all significant SNPs considered together was equal to 6.9% with a standard error of 0.02. In chickens, the effect of
significant SNPs on bodyweight was reported between 3% and 8.1% [30, 31] and our results would appear to be similar to those found in this species.

As shown in Table 2, 27 significant SNPs out of the 33 identified in this study were mapped to 37 genes based on the Turkey 5.1 assembly [24] and the 15 kb up- and downstream distances previously described. Some SNPs were mapped to two genes and this is due to the 15 kb up- and downstream distances. From these 37 genes there were 13 novel LOC-named genes, i.e. genes that have yet to be characterised. The remaining six SNPs were neither within nor near any gene (15 kb up- or downstream). The lack of ability to map these SNPs to a gene could be due to the quality of the turkey genome assembly which contains many uncharacterized regions. The failure to connect markers to genes has been previously reported in pigs and was attributed to the low quality of the assembly; and for this reason a wider window of up to 50 kb has been suggested to assign such unlocated SNPs to genes [32]. In the present study, we maintained the 15 kb threshold as we found it a more prudent approach given the smaller relative size of the turkey genome compared to that of other livestock species. Although we also reported the nearest genes to these 6 SNPs in Table 3.
The 8 SNPs significantly associated with bodyweight on MGA 1 were located between 53.8 Mb and 182.3 Mb on the turkey genome shown in Table 1 and found to be distributed into two LD blocks that is depicted in Fig 3A. SNPs M2013, which is the leading SNP, and M2015 had a strong LD constructing a 52 kb long LD block (Block 1; Fig 3A). These two SNPs are located within \textit{AKR1D1} and \textit{PARP12} genes, respectively (Table 2). A third gene, which is the novel gene LOC100548731, is near M2015 and located 3,594 bp downstream of it. The \textit{AKR1D1} gene is a key gene that plays a critical role in the synthesis of bile acid and the metabolism of steroid hormones (e.g. [33, 34]), and studies have shown that dietary supplementation of bile acids can affect the activity of intestinal and lipoprotein lipases leading to improvement of broiler chicken growth [35, 36].

\textit{PARP12} gene, on the other hand, is a polymerase family member and found to be involved in regulating fatty acid metabolism [37] as well as body weight gain and insulin resistance in rats [38].

The second LD block (146 kb) on MGA 1 includes 5 SNPs, once again shown in Fig 3A where the leading SNP was M2985 (Table 1). Except for M2987, the SNPs in this block were both located within genes and near (up- or downstream) other genes within the 15 kb regulatory distance considered in this study. The genes are \textit{LOC100551192}, \textit{CLDND1}, \textit{GPR15}, \textit{LOC100550884}, \textit{ILDR1}, \textit{CFAP44} and \textit{BOC}. The latter was also the nearest gene to M2987 (34 kb upstream; Table 3). The protein encoded by \textit{BOC} mediates cell-cell interactions between muscle precursor cells and promotes myogenic differentiation [39]. Such protein has been reported to be associated with bodyweight gain and obesity in mice [40]. The expression of \textit{CLDND1} gene alters the metabolism functions in the liver leading to the progression of liver diseases [41] and in a recently published study, Zhu et al. [42] indicated that the \textit{CLDND1} gene is associated with energy production and fat metabolism in laying ducks. Moreover, according to Yi et al. (2016), the deficiency of fat metabolism in the liver increases ammonia levels and subsequently growth performance [43] and body fat distribution in broilers [44].

Two significant SNPs on MGA 2 affect bodyweight (Fig 3B); both had a strong LD and were located within a haplotype block span of 23 kb which covers \textit{ADCY3}, \textit{CENPO} and \textit{NCOA1} genes (Table 2). Interestingly, studies have shown that mutation and loss of function...
in ADCY3 induces bodyweight gain in humans [45–47]. One LD block (154 kb) for three significant SNPs associated with bodyweight was detected on a candidate region on MGA 4 (Fig 3C) covering the gene SPR in addition to three novel genes (Table 2). All significant SNPs on MGA 7 showed a strong LD located with one block, which extends to 53 kb (Fig 3D). Based on the Turkey 5.1 assembly [24], five genes: PMS1, TRNAL-CAG, MSTN, C2orf88 and HIBCH, were located within this LD block (Table 2). It is noteworthy to mention that the MSTN gene encodes a secreted ligand of the transforming growth factor-beta superfamily of proteins and regulators of muscle growth in chickens [48].

Table 1. SNPs significantly associated with 18-week body weight in turkeys detected by GWAS based on a 65K SNP Illumina panel.

| Chr | SNP    | Location bp | A1  | A2  | MAF  | Estimated effect | SE  | P-value |
|-----|--------|-------------|-----|-----|------|-----------------|-----|---------|
| 1   | M2013  | 53847539    | G   | A   | 0.47 | -0.06           | 0.02| 2.2e-07 |
| 1   | M2015  | 53900019    | A   | G   | 0.27 | 0.06            | 0.02| 1.1e-06 |
| 1   | M2981  | 81173656    | G   | A   | 0.21 | -0.08           | 0.02| 3.6e-06 |
| 1   | M2982  | 81188549    | A   | C   | 0.20 | -0.09           | 0.02| 2.2e-06 |
| 1   | M2983  | 81222640    | A   | G   | 0.20 | -0.08           | 0.02| 6.6e-06 |
| 1   | M2985  | 81278334    | G   | A   | 0.20 | -0.08           | 0.02| 1.7e-06 |
| 1   | M2987  | 81320624    | A   | G   | 0.10 | -0.09           | 0.02| 1.8e-05 |
| 1   | M6708  | 182307763   | G   | A   | 0.26 | -0.05           | 0.01| 7.4e-06 |
| 2   | M10885 | 104288280   | G   | A   | 0.38 | -0.06           | 0.02| 6.9e-07 |
| 2   | M10886 | 104311936   | G   | A   | 0.38 | -0.05           | 0.02| 2.8e-06 |
| 3   | M13167 | 55687761    | G   | A   | 0.21 | 0.08            | 0.02| 3.2e-05 |
| 3   | M13195 | 56416803    | A   | G   | 0.36 | 0.08            | 0.02| 1.6e-07 |
| 4   | M16706 | 63350973    | C   | A   | 0.41 | -0.05           | 0.01| 1.3e-05 |
| 4   | M16744 | 64320934    | G   | A   | 0.40 | -0.06           | 0.01| 1.9e-08 |
| 4   | M16749 | 64455195    | A   | G   | 0.40 | -0.06           | 0.01| 9.0e-08 |
| 4   | M16750 | 64475756    | G   | A   | 0.37 | -0.05           | 0.01| 1.1e-06 |
| 7   | M23412 | 7123139     | G   | A   | 0.13 | -0.14           | 0.02| 1.4e-12 |
| 7   | M23413 | 7139162     | G   | A   | 0.13 | -0.15           | 0.02| 5.6e-13 |
| 7   | M23414 | 7146253     | C   | A   | 0.13 | -0.14           | 0.02| 2.9e-12 |
| 7   | M23415 | 7156975     | G   | A   | 0.13 | -0.15           | 0.02| 2.1e-13 |
| 7   | M23416 | 7176912     | A   | G   | 0.13 | -0.12           | 0.02| 1.1e-09 |
| 12  | M33976 | 318853      | A   | G   | 0.30 | 0.08            | 0.02| 1.4e-09 |
| 12  | M33982 | 1933794     | A   | G   | 0.30 | 0.08            | 0.02| 7.4e-08 |
| 12  | M34000 | 2325482     | A   | G   | 0.41 | -0.09           | 0.02| 1.5e-07 |
| 12  | M34622 | 8352581     | G   | A   | 0.42 | -0.08           | 0.02| 3.0e-06 |
| 12  | M34632 | 8423789     | C   | A   | 0.18 | 0.11            | 0.03| 1.4e-06 |
| 12  | M34634 | 8436955     | G   | A   | 0.18 | 0.10            | 0.03| 3.2e-06 |
| 12  | M34635 | 8443676     | A   | G   | 0.18 | 0.11            | 0.03| 2.5e-07 |
| 12  | M34673 | 8729360     | A   | G   | 0.15 | 0.11            | 0.03| 1.9e-05 |
| 12  | M34677 | 8758783     | A   | C   | 0.15 | 0.11            | 0.03| 8.8e-06 |
| 12  | M34679 | 8773696     | A   | G   | 0.15 | 0.11            | 0.03| 3.3e-05 |
| 12  | M34687 | 8829374     | A   | C   | 0.15 | 0.12            | 0.03| 5.8e-06 |
| 12  | M34688 | 8834569     | A   | G   | 0.15 | 0.12            | 0.03| 3.3e-06 |

1Chr = Chromosome  
2A1 = Major allele  
3A2 = Minor allele; 3MAF = Minor allele frequency  
4SE = Standard error.

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Table 2. Genes associated (within 15kbp) with SNPs significantly associated with 18-week bodyweight in female turkeys detected by GWAS based on a 65K SNP Illumina array.

| SNP     | Chromosome | Position (bp) | Location | Gene name   | Entrez  |
|---------|------------|---------------|----------|-------------|---------|
| M2013   | 1          | 53847539      | Within   | AKR1D1      | 100547967 |
| M2015   | 1          | 53900019      | Within   | PARP12      | 100548121 |
| M2015   | 1          | 53900019      | 3594 D   | LOC100548731 | 100548731 |
| M2981   | 1          | 81173656      | 6068 U   | LOC100551192 | 100551192 |
| M2981   | 1          | 81173656      | Within   | CLDN1       | 100550575 |
| M2981   | 1          | 81173656      | 13216 D  | GPR15       | 100550729 |
| M2982   | 1          | 81188549      | 8105 U   | CLDN1       | 100550575 |
| M2982   | 1          | 81188549      | Within   | GPR15       | 100550729 |
| M2982   | 1          | 81188549      | 13123 D  | LOC100550884 | 100550884 |
| M2983   | 1          | 81222640      | 995 U    | ILDR1       | 100551346 |
| M2983   | 1          | 81222640      | Within   | CFAP44      | 100538354 |
| M2985   | 1          | 81278334      | Within   | BOC         | 100538508 |
| M6708   | 1          | 182307763     | Within   | UVRAG       | 100544950 |
| M10885  | 2          | 104288280     | 7357 U   | ADCY3       | 100538467 |
| M10885  | 2          | 104288280     | 310 U    | CENPO       | 100538621 |
| M10886  | 2          | 104311936     | 794 D    | NCOA1       | 100538778 |
| M13167  | 3          | 55687761      | Within   | LOC104910342 | 104910342 |
| M13195  | 3          | 56416803      | 1232 U   | CHCHD7      | 100538622 |
| M13195  | 3          | 56416803      | 693 U    | SDR16C5     | 100538468 |
| M16706  | 4          | 63330973      | 14095 U  | LOC100544079 | 100544079 |
| M16706  | 4          | 63330973      | 10800 U  | LOC116216609 | 116216609 |
| M16706  | 4          | 63330973      | 78 U     | LOC109367489 | 109367489 |
| M16706  | 4          | 63330973      | 5350 D   | LOC100544391 | 100544391 |
| M16744  | 4          | 64320934      | 5020 U   | LOC104909285 | 104909285 |
| M16744  | 4          | 64320934      | 10844 D  | LOC100544235 | 100544235 |
| M16749  | 4          | 64455195      | Within   | LOC104910910 | 104910910 |
| M16750  | 4          | 64475756      | 12094 D  | SPR         | 100542371 |
| M23412  | 7          | 7123139       | 11509 U  | PMS1        | 100543933 |
| M23412  | 7          | 7123139       | 8842 D   | TRNAL-CAG   | 109368711 |
| M23413  | 7          | 7139162       | 7099 U   | TRNAL-CAG   | 109368711 |
| M23413  | 7          | 7139162       | 12568 D  | MSTN        | 100303659 |
| M23414  | 7          | 7146253       | 14190 U  | TRNAL-CAG   | 109368711 |
| M23414  | 7          | 7146253       | 5477 D   | MSTN        | 100303659 |
| M23414  | 7          | 7146253       | 10964 D  | C7H2orf88   | 104911634 |
| M23415  | 7          | 7165975       | 8641 U   | MSTN        | 100303659 |
| M23415  | 7          | 7165975       | Within   | C2orf88     | 104911634 |
| M23416  | 7          | 7176912       | Within   | C2orf88     | 104911634 |
| M23416  | 7          | 7176912       | 8571 D   | HIBCH       | 100544087 |
| M33976  | 12         | 318853        | Within   | RBPMS2      | 100539257 |
| M33982  | 12         | 1933794       | 7167 D   | HMG20A      | 100538822 |
| M34000  | 12         | 2325482       | Within   | LOC100549019 | 100549019 |
| M34622  | 12         | 8352581       | Within   | AP4E1       | 100539719 |
| M34622  | 12         | 8352581       | 3086 D   | TNAFAP8L3   | 100539875 |
| M34632  | 12         | 8423789       | Within   | LOC100549427 | 100549427 |
| M34634  | 12         | 8436955       | 2302 U   | LOC100549427 | 100549427 |
| M34634  | 12         | 8436955       | 14598 D  | GLDN        | 100540031 |

(Continued)
Fifteen significant SNPs associated with bodyweight were found on MGA 12, which was the highest number of significant SNPs on a single chromosome in this study (Tables 2 and 3). Five out of these 15 SNPs were not located near any gene within the 15 kb distance (Table 3). The LD analysis indicated that 8 SNPs had a strong LD ($r^2 \geq 0.97$) located within a single 410 kb long LD block. Whereas the first 3 SNPs in this block cover two genes (GLDN and LOC100549427) within the 15 kb distance (Table 2), the last 5 SNPs were positioned near SEMA6D and LOC116217089 genes but were beyond the 15 kb distance (Table 3). The HMG20A gene plays an important role in obesity in human [49, 50] and mice [51]. The TNFAIP8L3 gene was reported to affect growth and backfat thickness in pigs [52].

Finally, the distance between the two significant SNPs on MGA 3 was more than 729 kb. The first SNP, M13167, was within the novel gene LOC104910342, and the second SNP, M13195, was upstream of SDR16C5 (693 bp) and CHCHD7 (1,232 bp) genes. Nishimura et al. [53] indicated that CHCHD7 was significantly associated with carcass weight in Japanese black cattle, and recently Edea et al. [54] reported that SDR16C5 gene is associated with weaning weight, yearling weight and bodyweight gain in Korean cattle breeds.

### Conclusions

In this study, we performed a GWA study for 18-weeks bodyweight in female turkeys using a 65K SNP array. The results revealed that 33 SNPs were significantly associated with this trait based on a 5% FDR. The linkage disequilibrium analysis showed that most of these genes are grouped into blocks that extend up to 410 kb. The significant SNPs were mapped to 37 genes, of which 13 were novel. Most of the genes detected are involved in functions related to body-weight and growth, which has been supported by gene network analyses. The functions of the significant genes included regulation of growth, metabolism, digestion, bile acid biosynthetic and development of muscle cells. These findings could contribute to a better understanding of the genetic architecture of body weight gain in turkeys. However, further examination is required to prove the novel genes discovered in this study as putative genes for body weight in female turkeys.
Supporting information

S1 Fig. A quantile–quantile plot from GWAS for 18-week body weight in turkeys using a 65K SNP Illumina panel for all SNPs (dark blue) and after excluding SNPs significantly (false discovery rate of 5%) associated with the trait (black). The sharp deviation above an expected -log10 p-value of approximately 3 is due to a strong association of 18-week body weight in turkeys with significant SNPs. Exclusion of significantly associated SNPs may leave a residual upward deviation leading to identify more associated SNPs with the trait, which was not the case in this study.

(TIF)

S2 Fig. A quantile–quantile plot from GWAS for 18-week body weight in turkeys using a 65K SNP Illumina panel with adjustment for population stratification using the two top principal components (light blue) and without adjustment (dark blue). The adjustment for population stratification did not change the findings of this GWAS study. The population used in this study is a pure turkey line and confounding due to population subgroups is unlikely to be observed.

(TIF)
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References

1. FAO. FAOSTAT [Internet]. 2021 [cited 2021 Feb 3]. Available from: http://www.fao.org/faostat/en/
data/QL/visualize
2. Baldi A, Gottardo D. Livestock Production to Feed the Planet: Animal Protein: A Forecast of Global Demand over the Next Years. Rel Beyond Anthr. 2017; 5:65.
3. Salter AM. Improving the sustainability of global meat and milk production. Proc Nutr Soc. 2017; 76 (1):22–7.
4. Aslam ML, Bastiaansen JWM, Crooijmans RPMA, Vereijken A, Groenen MAM. Whole genome QTL mapping for growth, meat quality and breast meat yield traits in turkey. BMC Genet. 2011; 12(1):1–10.
5. Abdalla EA, Schenkel FS, Emamgholi Begli H, Willems OW, van As P, Vanderhout R, et al. Single-Step Methodology for Genomic Evaluation in Turkeys (Meleagris gallopavo). Front Genet [Internet]. 2019 Dec 20 [cited 2020 Jan 4];10. Available from: https://www.frontiersin.org/article/10.3389/fgene.2019.01248/full
6. Abdalla EA, Wood BJ, Baes CF. Accuracy of breeding values for production traits in turkeys (Meleagris gallopavo) using recursive models with or without genomics. Genet Sel Evol. 2021; 53(1):1–10.
7. Nestor KE. Genetics of Growth and Reproduction in the Turkey.: 9. Long-Term Selection for Increased 16-Week Body Weight. Poult Sci [Internet]. 1984 Nov 1 [cited 2019 May 9]; 63(11):2114–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/6514659
8. Nestor KE, Anderson JW, Patterson RA. Genetics of Growth and Reproduction in the Turkey. 14. Changes in Genetic Parameters Over Thirty Generations of Selection for Increased Body Weight. Poult Sci [Internet]. 1999; 78(1):337–47. Available from: http://ps.oxfordjournals.org/cgi/doi/10.3382/ps.056337
9. Nestor KE, Anderson JW, Patterson RA, Velleman SG. Genetics of growth and reproduction in the turkey. 17. Changes in genetic parameters over forty generations of selection for increased sixteen-week body weight. Poult Sci. 2008; 87(10):1971–9.
10. Emamgholi Begli H, Wood BJ, Abdalla EA, Balzani A, Willems O, Schenkel F, et al. Genetic parameters for clutch and broodiness traits in turkeys (Meleagris Gallopavo) and their relationship with body weight and egg production. Poult Sci [Internet]. 2019 Aug 12 [cited 2019 Sep 3]; Available from: https://academic.oup.com/ps/advance-article/doi/10.3382/ps/p ez446/5548939
11. Goddard ME, Hayes BJ. Mapping genes for complex traits in domestic animals and their use in breeding programmes. Nat Rev Genet. 2009; 10(6):381–91.
12. Georges M. Mapping, fine mapping, and molecular dissection of quantitative trait loci in domestic animals. Annu Rev Genomics Hum Genet. 2007; 8:131–62.
13. Berri C, Wacrenier N, Millet N, Le Bihan-Duval E. Effect of selection for improved body composition on muscle and meat characteristics of broilers from experimental and commercial lines. Poult Sci. 2001; 80 (7):833–8.
14. Guo Y, Qiu H, Xiao S, Wu Z, Yang M, Yang J, et al. A genome-wide association study identifies genomic loci associated with backfat thickness, carcass weight, and body weight in two commercial pig populations. J Appl Genet. 2017; 58(4):499–508. https://doi.org/10.1007/s13353-017-0405-6 PMID: 28890999

15. Crispim AC, Kelly MJ, Guimarães SEF, e Silva FF, Fortes MRS, Wenceslau RR, et al. Multi-locus GWAS and new candidate genes annotation for growth curve parameters in Brahman cattle. PLoS One. 2015; 10(10):e0139906.

16. Heffner EL, Sorrells ME, Jannink J-L. Genomic selection for crop improvement. 2009;

17. Browning BL, Zhou Y, Browning SR. A One-Penny Imputed Genome from Next-Generation Reference Panels. Am J Hum Genet [Internet]. 2018 Sep [cited 2018 Nov 15]; 103(3):338–48. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0002929718302428 https://doi.org/10.1016/j.ajhg.2018.07.015 PMID: 30100085

18. Purcell S, Neale B, Todd-Brown K, Thomas L, Ferreira MAR, Bender D, et al. PLINK: a tool set for whole-genome association and population-based linkage analyses. Am J Hum Genet. 2011; 88(1):76–82.

19. Abdalla EA, Id-Lahoucine S, Cánovas A, Casellas J, Schenkel FS, Wood BJ, et al. Discovering lethal alleles across the turkey genome using a transmission ratio distortion approach. Anim Genet. 2020; https://doi.org/10.1111/age.13003 PMID: 33006154

20. Yang J, Weedon MN, Purcell S, Lettre G, Estrada K, Willer CJ, et al. Genomic inflation factors under polygenic inheritance. Eur J Hum Genet. 2011; 19(7):807–12.

21. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J R Stat Soc Ser B. 1995; 57(1):289–300.

22. R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/

23. Yang J, Lee SH, Goddard ME, Visscher PM. GCTA: a tool for genome-wide complex trait analysis. Am J Hum Genet. 2011; 88(1):76–82.

24. Dalloul RA, Long JA, Zimin AV, Aslam L, Beal K, Blomberg LA, et al. Multi-platform next-generation sequencing of the domestic Turkey (Meleagris gallopavo): Genome assembly and analysis. Roberts RJ, editor. PLoS Biol [Internet]. 2010 Sep 7 [cited 2019 Jan 5]; 8(9):e1000475. Available from: https://dx.plos.org/10.1371/journal.pbio.1000475

25. Rao YS, Liang Y, Na Xia M, Shen X, Jun Du Y, Gong Luo C, et al. Extent of linkage disequilibrium in wild and domestic chicken populations. Hereditas. 2008; 145(5):251–7.

26. Qanbari S, Hansen M, Weigend S, Preisinger R, Simianer H. Linkage disequilibrium reveals different demographic history in egg laying chickens. BMC Genet. 2010; 11(1):103.

27. Megens H-J, Crooijmans RPM, Bastiaansen JWM, Kerstens HHD, Coster A, Jalving R, et al. Comparison of linkage disequilibrium and haplotype diversity on macro- and microchromosomes in chicken. BMC Genet. 2009; 10(1):86.

28. Hinrichs AL, Larkin EK, Suarez BK. Population stratification and patterns of linkage disequilibrium. Genet Epidemiol. 2009; 33(S1):S88–92.

29. Price AL, Zaitlen NA, Reich D, Patterson N. New approaches to population stratification in genome-wide association studies. Nat Rev Genet. 2010; 11(7):459–63.

30. Gu X., Feng C., Ma L., Song C., Wang Y., Da Y., et al. Genome-wide association study of body weight in chicken F2 resource population. PLoS One 6:e21872.

31. Van Goor A., Bolek K.J., Ashwell C.M., Persia M.E., Rothschild M.F., Schmidt C.J., et al. Identification of quantitative trait loci for body temperature, body weight, breast yield, and digestibility in an advanced intercross line of chickens under heat stress. Genet. Sel. Evol. 47:96.

32. Mebratie W, Reyer H, Wimmers K, Bovenhuys H, Jensen J. Genome-wide association study of body weight and feed efficiency traits in a commercial broiler chicken population, a re-visitiation. Sci Rep. 2019; 9(1):1–10.

33. Valanejad L, Ghareeb M, Shiffka S, Nadolny C, Chen Y, Guo L, et al. Dysregulation of Δ4-3-oxosteroid 5β-reductase in diabetic patients: implications and mechanisms. Mol Cell Endocrinol. 2018; 470:127–41.

34. Chaudhry AS, Thirumaran RK, Yasuda K, Yang X, Fan Y, Strom SC, et al. Genetic variation in aldol-keto reductase 1D1 (AKR1D1) affects the expression and activity of multiple cytochrome P450s. Drug Metab Dispos. 2013; 41(8):1538–47.

35. Ge XK, Wang AA, Ying ZX, Zhang LG, Su WP, Cheng K, et al. Effects of diets with different energy and bile acids levels on growth performance and lipid metabolism in broilers. Poult Sci. 2019; 98(2):887–95.
36. Lai W, Huang W, Dong B, Cao A, Zhang W, Li J, et al. Effects of dietary supplemental bile acids on performance, carcass characteristics, serum lipid metabolites and intestinal enzyme activities of broiler chickens. Poult Sci. 2018; 97(1):196–202.

37. Dunnick JK, Morgan DL, Elmore SA, Gerrish K, Pandiri A, Ton T V, et al. Tetramethylbenzidine A activates the hepatic interferon pathway in rats. Toxicol Lett. 2017; 266:32–41.

38. Bai P, Canto C, Brunyánszki A, Huber A, Szántó M, Cen Y, et al. PARP-2 regulates SIRT1 expression and whole-body energy expenditure. Cell Metab. 2011; 13(4):450–60. https://doi.org/10.1016/j.cmet.2011.03.013 PMID: 21425329

39. O’Leary NA, Wright MW, Brister JR, Ciufio S, Haddad D, McVeigh R, et al. Reference sequence (RefSeq) database at NCBI: Current status, taxonomic expansion, and functional annotation. Nucleic Acids Res [Internet]. 2016 Jan 4 [cited 2018 Nov 28]; 44(D1):D733–45. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26553804 https://doi.org/10.1093/nar/gkv1189 PMID: 26553804

40. Lee H-J, Jo S-B, Romer AI, Lim H-J, Kim M-J, Koo S-H, et al. Overweight in mice and enhanced adipogenesis in vitro are associated with lack of the hedgehog coreceptor boc. Diabetes. 2015; 64(6):2092–103. https://doi.org/10.2337/db14-1017 PMID: 25576054

41. Zhu C, Xu W, Tao Z, Song W, Liu H, Zhang S, et al. Effects of atmospheric ammonia on the production performance, serum biochemical indices, and liver RNA-seq data of laying ducks. Br Poult Sci. 2020; (just accepted).

42. Kletzien RF, Harris PKW, Foellmi LA. Glucose-6-phosphate dehydrogenase: a “housekeeping” enzyme subject to tissue-specific regulation by hormones, nutrients, and oxidant stress. FASEB J. 1994; 8(2):174–81. https://doi.org/10.1096/fasebj.8.2.811948 PMID: 8119488

43. Yahav S. Ammonia affects performance and thermoregulation of male broiler chickens. Anim Res. 2004; 53(4):289–93.

44. Yi B, Chen L, Sa R, Hong R, Xing H, Zhang H. Transcriptome profile analysis of breast muscle tissues from high or low levels of atmospheric ammonia exposed broilers (gallus gallus). PLoS One. 2016; 11(9):e0162631. https://doi.org/10.1371/journal.pone.0162631 PMID: 27611572

45. Saeed S, Bonnefond A, Tamanini F, Mirza MU, Manzoor J, Janjua QM, et al. Loss-of-function mutations in ADCY3 cause monogenic severe obesity. Nat Genet. 2018; 50(2):175–9. https://doi.org/10.1038/s41588-017-0023-6 PMID: 29311637

46. Reshetnikov E, Abramova M, Ponomarenko I, Polonikov A, Verzilina I, Sorokina I, et al. Dataset of allele and genotype frequencies of five polymorphisms candidate genes analyzed for association with body mass index in Russian women. Data Br. 2020; 28:104962.

47. Abu-Taweel GM, Rajagopal R, Sun-Ju K, Kim H-J, Kim YO, Mothana RA, et al. Betulinic acid lowers lipid accumulation in adipocytes through enhanced NCoA1–PPARγ interaction. J Infect Public Health. 2019; 12(5):726–32. https://doi.org/10.1016/j.jiph.2019.05.011 PMID: 31133421

48. Guernec A, Chevalier B, Duclos MJ. Nutrient supply enhances both IGF-I and MSTN mRNA levels in chicken skeletal muscle. Domest Anim Endocrinol. 2004; 26(2):143–54. https://doi.org/10.1016/j.dame.2003.10.001 PMID: 14757186

49. Shahid SU, Li KW, Acharya J, Cooper JA, Hasnain S, Humphries SE. Effect of six type II diabetes susceptibility loci and an FTO variant on obesity in Pakistani subjects. Eur J Hum Genet. 2016; 24(6):903–10. https://doi.org/10.1038/ejhg.2015.212 PMID: 26395551

50. Ashour E, Gouda W, Mageed L, Afify M, Hamimy W, Shaker YM. Evaluation of genetic susceptibility of six type II diabetes Genome-Wide association studies loci for obesity. Meta Gene. 2020; 26:100758.

51. Mellado-Gil JM, Fuente-Martín E, Lorenzo PI, Martín-Montalvo A, et al. The type 2 diabetes-associated HMG20A gene is mandatory for islet beta cell functional maturation. Cell Death Dis. 2018; 9(3):1–15. https://doi.org/10.1038/s41419-018-0272-z PMID: 29449530

52. Jiang Y, Tang S, Tang C, Wang Y, Chen J, Yang Y, et al. A genome-wide association study of growth and fatness traits in two pig populations with different genetic backgrounds. J Anim Sci. 2018; 96(3):806–16. https://doi.org/10.1093/jas/skx038 PMID: 29528397

53. Nishimura S, Watanabe T, Mizoshita K, Tatsuda K, Fujita T, Watanabe N, et al. Genome-wide association study identified three major QTL for carcass weight including the PLAG1-CHCHD7 QTN for stature in Japanese Black cattle. BMC Genet. 2012; 13(1):40. https://doi.org/10.1186/1471-2156-13-40 PMID: 22607022

54. Edea Z, Jung KS, Shin S-S, Yoo S-W, Choi JW, Kim K-S. Signatures of positive selection underlying beef production traits in Korean cattle breeds. J Anim Sci Technol. 2020; 62(3):293–305. https://doi.org/10.5187/jast.2020.62.3.293 PMID: 32568261