Expression QTL mapping for meat quality in beef cattle

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Intro and Objectives

- Expression QTL mapping provides information about genetic variant with modulatory effects on gene expression which are useful for understanding the **genetic architecture** of complex phenotypes.
- This mapping allows for uncovering of genomic regions associated with transcription regulation of genes which can be related to phenotypic variation when they colocalize with QTLs (cis and trans effects), providing a molecular basis for the phenotype-genotype association.
- **Objective:** Perform eQTL mapping for meat quality traits in longissimus dorsi muscle and to uncover genes whose expression is influenced by local or distant genetic variation.

Methods

- The *longissimus* muscle from 120 steers from the UF multibreed Angus-Brahman were used for phenotypic measurements and RNA extraction.
- Carcass measurements including marbling was recorded, and two 2.54 cm steaks were aged for 14 days. One steak was used for Warner Bratzler shear force (WBSF) and cooking loss, another for tenderness, juiciness and connective tissue by sensory panel.
- Principal component analysis for all phenotypes generated three principal components used to construct a meat quality index.
- Eighty animals selected based on extreme meat quality index for mRNA sequencing and 100 bp paired-end reads were mapped against to the Btau_4.6.1 assembly.
- A robust regression analysis identified gene and exons associated with meat quality. The association model accounted for population structure, normalized gene counts, and year of birth of the animal.
- A gene DE analysis was performed using the negative binomial distribution including breed group, year of birth and WBSF, tenderness or marbling as categorical variables.

Results

- Expression of 208 genes was associated with the meat quality index: *Rho GTPase Activating Protein 10* (*ARHGAP10*-**Figure 1A**), *Transmembrane Protein 120B* (*TMEM120B*-Figure 1B) and *Arrestin Domain Containing 4* (*ARRDC4*-**Figure 1C**).
- For WBSF 1,286 genes were DE (**Figure 2**). The most significant DE genes were *Zinc Finger DHHC-Type Containing 18* (*ZDHHC18*), *NFKB Inhibitor Interacting Ras Like 2* (*NKIRAS2*) and *Chondroitin Polymerizing Factor* (*CHPF*).
- A total of 9,491 eQTLs were discovered (**Figure 3**), the most frequently identified type was Trans-acting eQTLs.
- A total number of 23 polymorphisms distributed on 17 clusters were identified. The PDE8B gene was identified as the only master regulator with simultaneous • DiffTrans and Trans-acting regulation effect. **Figure 4** shows a network for the 23 master regulators and 620 regulated genes identified using eQTL associations.

Figure 3. eQTL mapping in *longissimus dorsi,* including 112,043 SNPs and 8,589 genes. Red arrows show hot spot clusters. DiffCis and DiffTrans associations were Cis or Trans eQTLs in TA or DE genes.
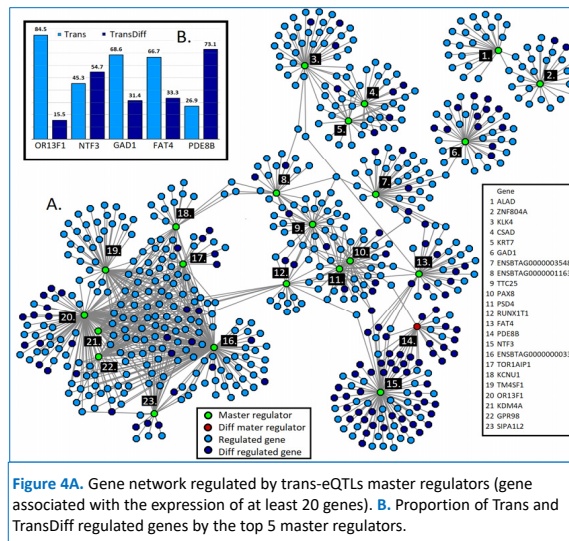
Figure 4A. Gene network regulated by trans-eQTLs master regulators (gene associated with the expression of at least 20 genes). **B.** Proportion of Trans and TransDiff regulated genes by the top 5 master regulators.

Figure 1. Regression analysis for **A.** ARHGAP10, **B.** TMEM120B and **C.** ARRDC4 using a meat quality index (tenderness, juiciness, connective tissue score, WBSF and marbling).

Figure 2. Significant differentially expressed genes (blue dots) in tough (high WBSF) versus tender (low WBSF) samples.

Conclusions

- Multiple cis eQTLs and sQTLs effects identified. LSM2, SOAT1, TTN and TEK are a few examples of potential expression and splicing regulatory genes.
- A total of 27 expression and 13 splicing master regulator genes uncovered: cytoskeletal or membrane-associated proteins, TF & DNA methylases.
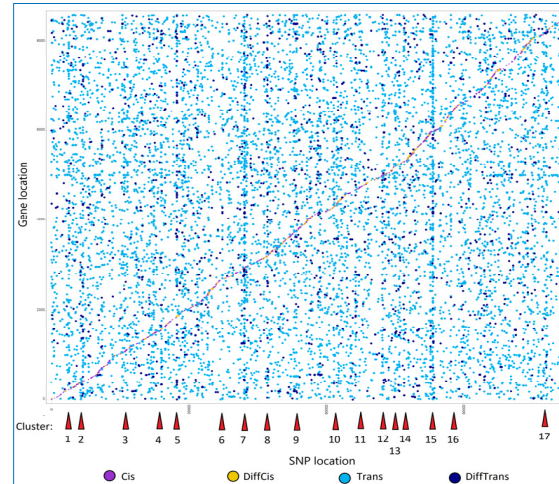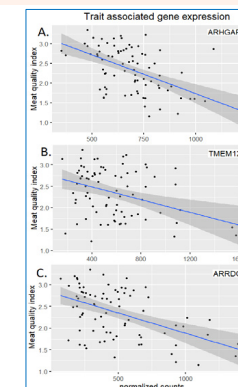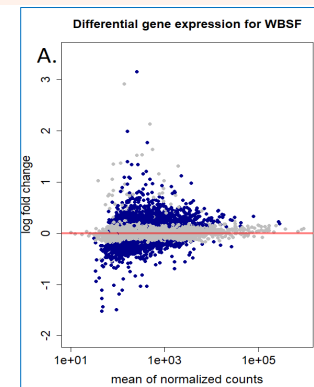
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