Meta-analysis of public transcriptomics data to understand and phenotype bovine body composition

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Take home message From a compilation of public genomics data, *HOXA5* was highlighted as a candidate driver or biomarker of bovine muscle mass accretion with age, in two bovine breeds, and for either steers or bulls.

Introduction Producing ruminant with adequate muscular and adipose tissues masses, *i.e.* lean-to-fat ratio, is an economic challenge for the bovine sector. The lean-to-fat ratio contribute to the animal adaptability, food efficiency and meat / carcass qualities. Despite numerous genomics studies that assayed how rearing factors affect the lean-to-fat ratio (Ceciliani *et al.*, 2018) there is no consensus on molecular biomarkers of the lean-to-fat ratio, perhaps due to the difficulty to compare large datasets produced with different quantitative protocols. One of the rare attempt to compile large datasets had merged micro-arrays data from a same quantitative protocol (Baron *et al.*, 2011). Our challenge is to compile public data and to implement statistical tools such as meta-analysis methods, to identify genes that could be robust biomarkers of the lean-to-fat ratio.

Materials & methods For datasets comparisons, we used R software, first to merge identifiers over datasets and to perform descriptive statistics with the ade4 package. We then used the metaMA package to look for differentially abundant genes in each study and whatever the studies (named Merged Data), by performing Benjamini-Hochberg corrections at a significant level of 5%. This pipeline was bench tested with 4 datasets from 2 transcriptomics studies of bovine *Longissimus* muscle (Qin *et al.*, 2011; Moisá *et al.*, 2013). These studies used different microarrays (UIUC Bos taurus 13.2K 70-mer condensed oligoarray and Affymetrix Bovine Genome Array), and cattle differing by the breed (Chinese Red Steppe vs Angus X Simmental), diet (compensatory growth plane of nutrition vs standard diet) and sex (steers vs bulls).

Results & discussion Only 855 GenBank accessions over thousands were shared by the 4 datasets. One gene (Homeobox protein Hox-A5, *HOXA5*), was overexpressed during muscle growth in each study and in the Merged Data (Figure 1), highlighting *HOXA5* as a potential marker of muscle accretion whatever the breed, diet and castration. The embryonic factor *HOXA5* has been found at the adulthood involved in fat depot in adipose tissue (Gesta *et al.*, 2006), but was never related to post-natal muscle biology. In dataset C, D and Merged Data, 179 genes were differentially abundant and may be drivers of muscle (including marbling) accretion with age. Of these, genes involved in *SMAD*, *TGF*-β or *activin* signalling already known to modulate muscle hypertrophy underscored the meta-analysis method.

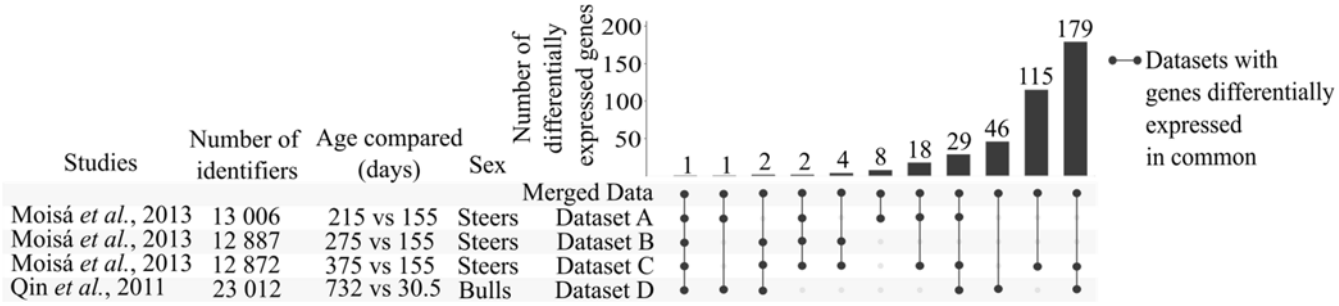

Figure 1 Descriptive data and number of differentially abundant genes in datasets used to bench test the meta-analysis.

Conclusion We provide methods to compile transcriptomics data that should foster the discovery of keys pathways or biomarkers of the lean-to-fat ratio, such as *HOXA5*. The next step is to increase the number of gene under compilation by a reannotation of transcriptomics data on the current bovine genome.

Acknowledgements The regional council of Auvergne-Rhône-Alpes and the Inra-Phase Division for funding J. Bazile.

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