Genome-wide methylation patterns in Holstein leukocytes

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Background

• Objective
  • Describe genome-wide DNA methylation patterns in Holsteins
    • Future: differences among cows with extreme phenotypes
• 8 lactating Holstein cows
• DNA extracted from peripheral blood leukocytes

MeDIP-seq

• ~100 million reads
  • BGI
• Paired-end 49-bp reads
• Initial alignment to bosTau4
  • 75% mapping rate, 46% unique
  • CpG
    • 78.4% ≥1 time (28.5% genome wide)
    • 19.8% ≥5 time (3.7% genome wide)

Reads

• Re-aligned to UMD 3.1
• Reads covering mapped nucleotides extracted
  • Geometric mean reads
• Merged with 13,677 Ensembl genes

GMR example

Average Genome?

<table>
<thead>
<tr>
<th></th>
<th>Breeding Value</th>
<th>Direct Genomic Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk yield kg</td>
<td>+413</td>
<td>+130</td>
</tr>
<tr>
<td>Fat yield kg</td>
<td>-6.4</td>
<td>-9.1</td>
</tr>
</tbody>
</table>
Genome-wide distribution

- Lower at centromeric end
  - 0.13 GMR first 500kb
  - 0.51 GMR last 500 kb, 0.47 GMR middle
- Higher in gene dense regions
  - Rank correlation 0.46 with number of genes in MB
- Partially methylated domains evident
  - 244.1 total MB
  - Olfactory Transduction genes overrepresented

Gene distribution (n=13,677)

Associations with Leukocyte Transcriptome Expression

GEO accession: GSE48487; Huang et al., 2012

Upstream GMR

Summary

- DNA methylation variable within and across chromosomes
  - Higher in gene rich regions
- Gene region methylation levels
  - Nadir ~100 bp upstream of transcription start site
  - Lower for initial exons and beginning of initial introns
  - Higher near intron/exon junctions than mid-intron
  - Higher mid-exon
- High levels in initial portion of genes associated with lower expression
Thanks for your attention