D17 - Allele specific expression analysis in bovine muscle tissue

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Short Abstract: Imprinted genes have been target of many studies, mainly in human and mouse, and lately in bovines due to the interest of understanding the epigenetic mechanisms underlying important meat quality phenotypes and the possibility of applying it in animal breeding programs in the future. Genomic DNA from 146 steers was genotyped using the Illumina BovineHD BeadChip in order to identify heterozygous individuals with known allele origin. Total mRNA from muscle was extracted and sequenced by Illumina HiScanSQ. The software ALEA was used to create a diploid genome for each individual, in which haplotype regions were reconstructed from the individual haplotypes. ALEA also maps short sequencing reads to the in silico genome constructed and detects reads that are uniquely aligned only to one of the two haploid genomes. In-house software was developed to compute the frequency of reads mapped to each allele and to perform binomial statistical tests in order to identify allele specific expression. From 742,906 SNPs contained in the Illumina BovineHD BeadChip, 419 were assigned to be imprinted based on the following criteria: heterozygous in the individual, homozygous in its sires, at least 20x RNA-Seq coverage, and $p<0.05$ for the statistical test. The Ensembl software VeP (Variant Effect Predictor) was used to determine the effect of these SNPs on genes, transcripts, and protein sequence, as well as regulatory regions. The VeP report together with phenotype information of the steers will be carefully examined in order to elucidate the molecular mechanisms involved with beef quality.

TOP

D18 - Cross-talk between intragenic epigenetic modifications and exon usage across developmental stages of human cells

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Short Abstract: Differential exon usage has been reported to affect the large majority of genes in mammalian genomes. It has been shown that different splice forms sometimes have distinctly different protein function. Here, we present an analysis of the Human Epigenome Atlas (version 8) to connect the differential usage of exons in various developmental stages of human cells/tissues to differential epigenetic modifications at the exon level. We found that the differential incidence of protein isoforms across developmental stages is often associated with changes in histone marks as well as changes in DNA methylation in the gene body or the promoter region. Many of the genes that are differentially regulated at the exon level were found to be associated with development and metabolism

TOP

D19 - Comprehensive analysis of chromatin landscape in filamentous fungus Aspergillus nidulans

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Short Abstract: Chromatin organisation, such as the deposition of active or repressive histone modifications, plays an important role in regulating gene expression. Advances in ChIP-seq and associated bioinformatics techniques have enabled genome-wide analysis of chromatin modification and transcription regulation dynamics. The chromatin landscape of human, mouse, and several model organisms have been widely studied, but other medically and biotechnologically important species, including many fungal species, are not yet fully studied. Here we present a genome-wide chromatin landscape of an important filamentous fungal model organism, Aspergillus nidulans. Using ChIP-seq, we generated genome-wide profiles of H3, H3K4me3, H3K4me1, H3K27ac, H3K9me3, H3K9ac, PolII and transcription factors in A. nidulans under different nutrient availability and quality as a novel approach to dissect the regulation of cellular metabolic homeostasis. We used a recently developed hierarchically linked infinite hidden Markov model (hiHMM) to systematically discover and characterise the most prevalent combination of histone modifications, i.e., chromatin state.

Our analysis revealed an interesting new chromatin state that consists of both H3K9me3 and H3K27ac, and is associated with gene repression. This state is covering 15-20% of the genome, and is located most prevalently in sub-telomeric regions, covering secondary metabolism and transmembrane transport genes. In addition, 10-20% of the genome are marked by classical enhancer chromatin marks, suggesting that these previously uncharacterised regions may have potential regulatory functions. Our work represents a valuable resource in A. nidulans that opens new avenues for investigation of the dynamic chromatin organisation and gene regulation in fungi.

TOP

D20 - Predicting long-range chromatin interactions using the genetic sequence

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Short Abstract: With Hi-C, a genome-wide analysis of chromatin interaction profiles is now possible. These interactions comprise pairs of loci that are close spatially, but not necessarily close in the sequence. This spatial co-localization of different chromosomal regions (cis as well as trans) can be due to a complex combination of factors viz. specific, direct contacts between two loci, nonspecific binding as a result of the packing of the chromatin fibre or co-localization due to functional association or having the same subnuclear structure.

In this work we show that the underlying genomic sequence at these loci is predictive of the long-range chromatin interactions involving these loci. We achieve this by casting it into a binary classification problem -- using a string kernel to measure similarity between the genomic sequences and a support vector classifier to classify a given set of linearly distal regions into spatially proximal or distal with respect to a particular TSS-containing region. In the first part we use the oligomer distance histograms kernel over the sequences and train an SVM downstream, while in the second we build a more sophisticated model with multiple kernels over putative fragments of these sequences thus capturing the hypothesized combinational mechanisms of interaction. Additionally, we exploit the sequences and their putative causal fragments to further improve the classification performance by employing multiple kernel learning to obtain the optimal weighting for kernels and multiple instance learning to accommodate for the lack of knowledge on the definite causal fragment(s). Our computational experiments also provide meaningful insights.

TOP

D21 - Medulloblastoma regulatory circuitries reveal subgroup-specific cellular origins

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