ISAG 2017

36th International Society for Animal Genetics Conference

16th - 21st July 2017

University College Dublin | Ireland

Bioinformatics · Comparative Genomics · Computational Biology
Epigenetics · Functional Genomics · Genome Diversity · Geno
Genome Sequencing · Immunogenetics · Integrative Geno
Microbiomics · Population Genomics · Systems Biolog
Genetic Markers and Selection · Genetics and Dis
Gene Editing · Bioinformatics · Comparative
Computational Biology · Epigenetics · Fun
Genome Diversity · Genome Sequenc
Integrative Genomics · Microbiom
Population Genomics · Syste
Genetic Markers and Sel
Genetics and Diseas
Gene Editing · Bi
Bioinformati

Genomes to Phenomes

O'Brien Centre for Science
and O'Reilly Hall,
University College Dublin,
Dublin, Ireland

ABSTRACT BOOK

www.isag.us/2017

@isagofficial #ISAG2017

many are unique when compared with known enhancer motifs in humans, indicative of sequence divergence between species. These data provide a basis for regulatory landscape comparison among sheep cell types and for cross-species comparative regulome analysis in macrophages and immune cells.

Key Words: ChIP-seq, H3K27ac, sheep, enhancers

163 The reconstruction and evolutionary history of eutherian chromosomes. J. Kim[1], M. Farre[2], L. Auvil[3], B. Capitanu[3], J. Ma[4], H. A. Lewin[5], and D. M. Larkin*[1], [1]*Department of Biomedical Science and Engineering, Konkuk University, Seoul, Korea;* [2]*Royal Veterinary College, University of London, London, UK;* [3]*Illinois Informatics Institute, University of Illinois at Urbana-Champaign, Urbana, IL, USA;* [4]*Computational Biology Department, School of Computer Science, Carnegie Mellon University, Pittsburgh, PA, USA;* [5]*Department of Evolution and Ecology, University of California, Davis, CA, USA.*

Whole genome assemblies of 19 placental mammals and two outgroup species were used to reconstruct the order and orientation of synteny blocks in chromosomes of the eutherian ancestor and six other descendent ancestors leading to human. For ancestral chromosome reconstructions, we developed a new algorithm (DESCHRAMBLER) that probabilistically determines the adjacencies of syntenic blocks using chromosome-scale and fragmented genome assemblies. The reconstructed chromosomes of the eutherian, boreoeutherian and euarchontoglires ancestor each included >80% of the entire length of the human genome, while reconstructed chromosomes of the most recent common ancestor of simians, catarrhini, great apes, and humans and chimpanzees included >90% of human genome sequence. These high coverage reconstructions permitted reliable identification of chromosomal rearrangements over ~105 million years (My) of eutherian evolution. Orangutan was found to have eight chromosomes that were completely conserved in homologous sequence order and orientation with the eutherian ancestor, the largest number for any species. Ruminant artiodactyls had the highest frequency of intrachromosomal rearrangements, while interchromosomal rearrangements dominated in murid rodents. A total of 162 chromosomal breakpoints in evolution of the eutherian ancestral genome to the human genome were identified; however, the rate of rearrangements was significantly lower (0.80/My) during the first ~60 million years of eutherian evolution, then increased to greater than 2.0/My along the five primate lineages studied. Our results significantly expand knowledge of eutherian genome evolution and will facilitate greater understanding of the role of chromosome rearrangements in adaptation, speciation, and the aetiology of inherited and spontaneously occurring diseases.

Key Words: ancestral chromosome reconstruction, primates, human, chromosome evolution, algorithm

164 iTRAQ-based proteomic analysis reveals key proteins affecting muscle growth and lipid deposition in pig. Z. Wang*[1], P. Shang[1,2], Q. Li[3], L. Wang[1], H. Zhang[1], and C. Wu[1], [1]*China Agricultural University, Beijing, China;* [2]*Tibet Agriculture and Animal Husbandry University, Linzhi, China;* [3]*Anhui Academy of Agricultural Sciences, Hefei, China.*

Pig growth rate and meat quality that are the main economic traits may be involved in multiple genes and biological pathways. The Tibetan pig (TP) and Diannan Small Ear pig (DSP) are indigenous Chinese breeds; they have significantly lower growth rates, higher lipid deposition ability, and better meat quality than those of introduced pig breeds such as Yorkshire (YY) and Landrace (LL). Nowadays, the proteomic analysis is a powerful method to identify key functional genes for the complex quantitative traits. Parallel reaction monitoring (PRM) is a recent development in targeted mass spectrometry and involves the use of a quadrupole-equipped Orbitrap. In present study, the *longissimus dorsi* muscle tissues were collected from the TP, DSP, YY and LL pig breeds at the age of six month and were performed the iTRAQ-based quantitative proteome analysis. The protein expression obtained using iTRAQ analysis was confirmed by quantifying the expression levels of twelve selected proteins by a PRM-MS analysis. Totally, 4,815 peptides corresponding to 969 proteins were detected. Comparison of expression patterns between TP-DSP and YY-LL revealed 288 differentially expressed proteins (DEPs), of which 169 were up-regulated and 119 were down-regulated. Functional annotation suggested that 28 DEPs were related to muscle growth and 15 to lipid deposition. Protein interaction network predictions indicated that differences in muscle growth and muscle fibre morphology between TP-DSP and YY-LL breeds were regulated by ALDOC, ENO3, PGK1, PGK2, TNNT1, TNNT3, TPM1, TPM2, TPM3, MYL3, MYH4, and TNNC2, while those in lipid deposition ability were regulated by LPL, APOA1, APOC3, ACADM, FABP3, ACADVL, ACAA2, ACAT1, HADH, and PECI. Twelve DEPs (up-regulated: UQCRC1, ACAT1, ACADM, PECI, MYL3, NNT, ACAA2, TTN, and HADH; down-regulated: PRDX4, MYL1, and LDB3) were selected for the PRM to confirm the reliability of the iTRAQ analysis. The fold changes and *P* values for these proteins were significantly different between the TP-DSP and YY-LL groups at $P < 0.10$, which was in agreement with the findings of the iTRAQ analysis. Our expression profiles provide new insights into the key proteins involved in muscle growth and lipid deposition in the pig.

Key Words: iTRAQ, PRM, muscle growth, lipid deposition, pig

165 Hypothalamus transcriptome during the early rise in LH secretion related to puberty age in bull calves. J. Liron[1], M. Fernández*[2], A. Prando[3], A. Baldo[3], and G. Giovambattista[2], [1]*Center of Veterinary Research (CIVETAN, CONICET), Faculty of Veterinary Sciences, UNCPBA, Tandil, Buenos Aires, Argentina.;* [2]*Institute of Veterinary Genetics (IGEVET, CONICET), Faculty of Veterinary Sciences, National University of La Plata, La Plata, Buenos Aires, Argentina;* [3]*Cátedra de Zootecnia Especial (II Parte), Faculty of Veterinary Sciences, National University of La Plata, La Plata, Buenos Aires, Argentina.*

Cattle puberty influences reproduction rates and profitability. In pre-pubertal bull calves there is an early transient rise in gonadotropin secretion between 10 and 20 weeks of age. The early elevation in mean circulating concentrations of LH and FSH most likely causes the proliferation of Sertoli and Leydig cells, respectively. This post-natal gonadotropin rise is considered one of the main factors in determining the age at which bulls reach puberty. In order to enhance our knowledge about genes and regulatory pathways involved in this phenomenon, we characterised the hypothalamus transcriptome from six Angus calves along this early expression pattern of LH (4, 6, and 14 wk of age) using the RNA-Seq technology. Of 37 million RNA-Seq reads per sample generated using the Illumina HiSEqn 2000 sequencer, at least 95% were mapped to the customized reference genome BosTau6. The gene annotation revealed that 13,976 genes were expressed in the hypothalamus. Tophat2, EdgeR, DESEqn 2, Bioconductor and R packages were utilised to performed differential expression (DE) analysis between groups. We detected 915 DE genes (*P* adjusted values < 0.05). The top gene ontology term enrichment of the highest expressed genes in the hypothalamus included cellular synapse, ion channel complex, neuron projection and plasma membrane part (Cellular component category); cell-cell signalling, transmembrane transport, behaviour and organism process (Biological process); metal ion transmembrane transporter activity and neuropeptide hormone activity (Molecular function). Enrichment analysis identified 40 KEGG signicantly enriched pathways. Based on the observation of the lowest *P*-value, calcium, oxytocin, circadian entrainment, cholinergic, glutamatergic, dopaminergic, serotonergic and GABAergic synapse, GnRH, oestrogen, Rap1, MAPK, ErbB, Ras and cancer signalling and several drugs addiction were among the most significant enriched pathways. The list of highest DE genes includes

OTP, AVP, OXT, CRH and TH, known for their physiological roles associated with lactation and mammalian social behaviours.

Key Words: cattle, functional genomics, RNA-seq, puberty, genetic improvement

166 Integrative genomics of human and bovine tuberculosis. K. E. Killick*[1,2], M. P. Mullen[3], T. Hall[1], N. C. Nalpas[4], I. W. Richardson[5], D. A. Magee[1], C. N. Correia[1], J. A. Browne[1], D. P. Berry[6], D. Bradley[7], V. Naranbhai[8], A. Hill[8], E. Gormley[9], S. V. Gordon[2,9], D. E. MacHugh[1,2], [1]*University College Dublin, UCD College of Health and Agricultural Sciences, University College Dublin, Dublin, Ireland;* [2]*University College Dublin, UCD Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Dublin, Ireland;* [3]*Athlone Institute of Technology, Department of Life and Physical Sciences, Athlone Institute of Technology, Athlone, Ireland;* [4]*University of Tübingen, Quantitative Proteomics and Proteome Centre Tübingen, Interfaculty Institute for Cell Biology, University of Tübingen, Tübingen, Germany;* [5]*IdentiGEN Ltd, IdentiGEN Ltd., Blackrock Business Park, Blackrock, Dublin, Ireland;* [6]*Teagasc, Animal and Grassland Research and Innovation Centre, Teagasc, Moorepark, Fermoy, Cork, Ireland;* [7]*Trinity College, Smurfit Institute of Genetics, University of Dublin, Trinity College, Dublin, Ireland;* [8]*University of Oxford, Wellcome Trust Centre for Human Genetics, Nuffield Department of Medicine, University of Oxford, Oxford, UK;* [9]*University College Dublin, UCD School of Veterinary Medicine, University College Dublin, Belfield, Dublin, Ireland.*

Human tuberculosis (TB), caused by *Mycobacterium tuberculosis*, is second only to HIV/AIDS as the greatest killer worldwide due to a single infectious agent. Bovine TB (BTB), caused by the closely related *Mycobacterium bovis* (99.95% sequence identity), is a major endemic disease affecting global cattle production, particularly in many developing countries. In the current study we used a network-based approach to integrate host gene expression data with high-density single-nucleotide polymorphism (SNP) genome-wide association (GWA) data to enhance detection of genomic variants for susceptibility/resistance to both *M. tuberculosis* and *M. bovis* infection. The host gene expression data used consisted of human and bovine RNA-seq data from macrophages infected with *M. tuberculosis* and *M. bovis*, respectively. A base gene interaction network of the mammalian host response to mycobacterial infection was generated using 213 genes identified from GeneCards (www.genecards.org). Differential gene expression data (FDR P value < 0.001) were superimposed on to this base network and the JActiveModules Cytoscape (www.cytoscape.org) plugin was used to extract functional modules with DE gene sets from macrophage infection experiments. SNP array population data was obtained from large human and bovine TB susceptibility/resistance studies, including the Wellcome Trust Case Control Consortium (WTCCC – www.wtccc.org.uk) resource and a published GWAS study in dairy cattle. SNPs from the top functional modules (5 kb up- and downstream of each gene) were identified for both human and bovine gene expression data. These analyses identified new genomic variants in humans and cattle associated with susceptibility and resistance to tuberculosis disease in both species. Comparison and integration of human and bovine gene expression data with GWAS data for TB and BTB can be used to identify shared and specific mechanisms underlying the mammalian host response to mycobacterial infection. In summary, the integrative genomics approach described here can be used to generate new knowledge by leveraging distinct but complementary omics datasets from a wide range of biological contexts.

Key Words: integrative genomics, bovine tuberculosis, mycobacterium tuberculosis

167 Circulating microRNAs as potential novel biomarkers to diagnose *Mycobacterium avium* ssp. *paratuberculosis* infection in cattle. K. Zhao[1], S. Hendrick[2], and L. Guan*[1], [1]*Department of Agricultural, Food and Nutritional Sciences, University of Alberta, Edmonton, AB, Canada;* [2]*Coaldale Veterinary Clinic, Lethbridge, Canada.*

Johne's disease (JD) is an infectious disease caused by *Mycobacterium avium* ssp. *paratuberculosis* (MAP) in ruminants. The circulating microRNAs are promising biomarkers for prediction and diagnosis of variety of diseases in humans. Therefore, the purpose of this study is to explore the potential of using the circulating microRNAs as diagnosis markers for early MAP infection detection. The microRNAomes of sera collected from three-year-old cows with clinical symptoms (CC, n = 20) and subclinical carriers (SC, n = 24) were generated using RNA-seq. In total, 116 expressed miRNAs were detected across all samples, and 11 of them were differentially expressed (DE) between CC and SC (fold change >2 and FDR < 0.05). Among them, seven miRNAs (miR-1468, 296–3p, 2284x, 2284y, 181a, 181b, and let-7f) were up-regulated in SC and four miRNAs (miR-192, 22–5p, 24–3p, and 361) were up-regulated in CC. Functional analysis showed that function of highly expressed miRNAs in SC was enriched to 'Metabolic pathway' by inhibiting the expression of genes related to glycolysis, fatty acid metabolism, and ATP synthesis. The function of those DE miRNAs in CC was enriched in 'Phagosome', including the genes regulate phagosome formation and function. Moreover, principal component analysis showed that sera miRNAome profiles of 24 SC cattle segregated into two groups (SC1 and SC2, n = 12, respectively), with profile of SC2 overlapped with those of the CC. This suggests that SC2 cattle may potentially progress to CC, while the SC1 may retain as SC. Moreover, 51 DE miRNAs were identified between SC1 and SC2 with 16 up-regulated in SC1 and 35 up-regulated in SC2. Functional analysis of up-regulated miRNAs in SC1 and SC2 showed similar pattern with those DE miRNAs between SC and CC, including 'Metabolic pathway' and 'Platelet activation'. Our results indicate that the decreased glucose/energy metabolism and innate immune response contributed partially to the molecular mechanism of MAP infection in SC and CC, respectively. The panels of circulating miRNAs (miR-2284x, 2284y, 181a, 181b, 24–3p, and 361) can be potentially used as novel biomarkers for early diagnosis of MAP infection at subclinical stage.

Key Words: biomarker, miRNAome, serum, Johne's disease

168 Generating customized integrated functional annotation datasets with BovineMine. C. Elsik*, D. Unni, A. Tayal, and D. Hagen, *University of Missouri, Columbia, Missouri, USA.*

BovineMine is the data mining resource of the Bovine Genome Database (BGD, http://BovineGenome.org). The objective of this presentation is to show how BovineMine can accelerate genomics research by enabling scientists without scripting skills to create and export customized annotation datasets merged with their own research data for use in downstream analyses. BovineMine allows researchers to leverage the curated gene pathways of model organisms (e.g. human, mouse and rat) based on orthology, and is especially useful for GO and pathway analyses in conjunction with GWAS and QTL studies. BovineMine also includes the reference genomes of sheep and goat so researchers can leverage information across ruminants. BovineMine uses the InterMine platform to integrate data from a variety of sources, including reference genome assemblies, genes (NCBI, Ensembl, Official Gene Set), proteins (UniProt), protein families and domains (InterPro), orthologs and paralogs (EnsemblCompara, Homologene, OrthoDB, TreeFam), pathways (BioCyc, KEGG, Reactome), interactions (BioGRID, IntAct), Gene Ontology (GO), QTL (AnimalQTLdb), variation (dbSNP, dbVar) and publications (PubMed). Pre-computed data from BGD, including variant effects and RNAseq-based gene expression, allow users to query tissue specific gene expression levels together with genomic variation data. BovineMine provides simple and sophisticated data mining tools. Built-in query templates pro-