Annual Report of Multistate Research Activity

PROJECT NUMBER: NRSP-8

PROJECT TITLE: NRSP-8: Cattle Species Genome Committee

PERIOD COVERED: January 1 to December 31, 2003

DATE OF THIS REPORT: February 5, 2004

ANNUAL MEETING DATE(S): January 11-12, 2004

PARTICIPANTS: Cattle/Sheep Workshop PAG XII, San Diego, CA Jan. 11 2004, 56 total participants, 20 with NRSP8 affilitiation (highlighted in green), the remainder non-affiliated visitors. Note, there were many more attendees at the sponsored talks. For a list of attendees see Appendix A (http://www.genome.iastate.edu/cattle/community/NRSP-8/PAG12_report.html).

BRIEF SUMMARY OF MINUTES OF ANNUAL MEETING: A major focus for many of the Cattle NRSP8 community has been to foster and promote the sequencing of the bovine genome. This effort has come to fruition, largely through the efforts of Jim Womack of Texas A&M University and Steven Kappes of USDA-MARC. Two of the sponsored talks provided updates on the current physical mapping effort for the bovine genome and the genome sequencing project itself. Unanimous election of Udaya DeSilva (Oklahoma State) as Cattle/Sheep Secretary, Milton Thomas (Current Secretary) to be Chairman of Cattle/Sheep Workshop at PAG 13 (Jan. 2005). See Appendix B for the detailed meeting agenda (http://www.genome.iastate.edu/cattle/community/NRSP-8/PAG12_report.html).

ACCOMPLISHMENTS AND IMPACTS:

Progress Toward Objective 1: *Enhance and integrate genetic and physical maps of agriculturally important animals for cross species comparisons and sequence annotation.*

The 5000 and 12,000 rad radiation hybrid panels generated in TX are freely distributed to investigators world wide. A collaboration between TX and IL has produced a second-generation 5000 rad radiation hybrid (RH) map of the cattle genome using cattle ESTs that were targeted to gaps in the existing cattle-human comparative map as well as to sparsely populated map intervals. A cattle-human comparative map containing 1463 comparative anchor points was then created using human genome sequence coordinates for the paired orthologs in order to define the boundaries of conserved chromosome segments. The new, more detailed cattle-human comparative map will provide a resource for the analysis of mammalian chromosome evolution and will facilitate the identification of candidate genes for economically important traits. In addition, An international consortium (including TX, IL, USDA-ARS) has been formed in order to create a sequence-ready comparatively anchored bacterial artificial chromosome (BAC) map of the cattle genome. The BAC clone-based comparative map provides a foundation for the evolutionary analysis of mammalian karyotypes and for sequencing of the cattle genome. Approximately 312,000 BAC end sequences are in the public domain as a result of this collaborative effort, and a minimal tiling path of BACs for the bovine genome sequencing project has been generated. Excellent progress has been made towards an integrated bovine map and the ultimate goal of a fully sequenced bovine genome. Specific regions of the bovine

genome have already been sequenced (TX), in particular, the genomic sequence for the class IIB and class III regions of the bovine MHC are at draft stage and nearing finished quality.

An *in silico* approach (CA) was developed to identify homologies existing between mapped cattle, pig, chicken and horse microsatellite flanking sequences and GenBank nucleotide sequences. A total of 67 bovine, 44 porcine, 21 chicken and 129 horse microsatellite flanking sequences had significant matches to human genomic sequence, genes or expressed sequence tags. These microsatellites were mapped in human providing useful links between the comparative maps of humans and livestock.

Future plans for the physical/comparative map include the goal of a 1MB resolution comparative map (TX, IL), a bovine HapMap (TX) and finished sequence for the class IIB and class III regions of the bovine MHC (TX). The bovine genome is currently being sequenced making sequence annotation and integration with map data a high priority.

Progress Toward Objective 2: *Facilitate integration of genomic, transcriptional, proteomic and metabolomic approaches toward better understanding of biological mechanisms underlying economically important traits.*

Work towards this objective includes ESTs, microarrays, QTL mapping and candidate gene evaluations for economically important traits. Over 3000 new ESTs (OSU) have been sequenced from bovine adipose tissue. A first generation bovine adipose tissue microarray comprised of 1100 unique cDNAs from these ESTs has been generated. An additional bovine microarray has been constructed (IA) that includes 10,604 unique bovine cDNAs from the BOV1-4 cDNA libraries. This array is now available for distribution to other investigators at a nominal cost. Transcriptional profiling using these arrays will allow identification of pathways and and candidate genes responsible for economically important traits.

QTL mapping for various traits is underway (TX, WI, IL, CA). In a genome-wide search (WI), the strongest evidence (chromosome-wise $P<0.01$) for a new ovulation rate QTL was found on chromosome 14. Evidence for this QTL was found in both families studied (two extended families whose patriarchs are paternal half-sib, Swedish Friesian sires). Efforts were conducted to replicate ovulation rate or twinning rate QTL effects in Holstein families. A total of 20 paternal half-sib sire families were used for this purpose. The families were chosen for study on the basis of patriarch PTA for twinning rate and the number of available sons. Two regions show evidence of QTL segregation in multiple families, and strong support for a previously reported BTA5 QTL (nominal $P=0.0003$) was found in a combined analysis of four, related families. Maternal reproductive traits are being investigated in a new set of families (TX) that are being generated. Currently 10 F2 families (Bos taurus x Bos indicus) planned with 20 females desired in each to evaluate female reproductive traits. Males will be used for feed efficiency experiments. At present there are 54 calves in 7 families and there are 212 embryo transfers pending and 209 frozen embryos. Continued characterization of high-growth rate mice (*hg*) has yielded increased understanding of the biological mechanisms underlying animal growth (CA). An integrative approach was employed For QTL dependent on the presence of *hg*. This approach combined the use of congenic strains with the bioinformatics-supported identification of candidate genes, which map within QTL regions and are involved in Gh signal transduction. This approach was aimed at increasing the speed in which modifier genes could be discovered by integrating data mining tools, sequences databases and defining the components of metabolic pathways. This integrated approach will lead to the molecular basis of growth QTL, shedding light on the mechanisms and biochemical pathways involved in the regulation of growth and body composition. A number of candidate genes for growth, disease resistance and reproduction have been evaluated in association studies (TX, NM). Mapping and identification of QTL provide the precursors for a better understanding of biological traits.

Future plans are aimed at using the above mentioned microarrays to identify candidates and pathways involved in economically important traits such as marbling and fatty liver disease in cattle. Ultimately, QTL data will be integrated with transcriptional profiling data to help identify QTL at the gene or nucleotide level. Next year, resource families will be expanded and additional phenotype and genotype data will be collected.

Progress Toward Objective 3: *Facilitate and implement bioinformatic tools to extract, analyze, store and disseminate information.*

Two groups have begun to implement QTL databases on the web for bovine QTL data (CA,TX). One strategy has been to use the Generic Genome Browser (http://www.gmod.org) as the front end for a MySQL database. The other strategy has been to use the RatMap QTL browser (http://ratmap.org/qtler/) as the basis for an improved interface. Both databases will contain public domain QTL data and one of them will feature password protected log on for investigators to edit or submit QTL data prior to publication.

Future plans include making the sites public once they have undergone final interface testing. The goal is to provide a site for investigators to deposit and retrieve up to date bovine QTL data. Ultimately these sites will be linked to the annotated bovine genome sequence.

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