326 Genome scan for quantitative trait loci for growth and reproductive traits in female mice. F. Siewerdt*[1,2], E. J. Eisen[1], and D. Pomp[3], [1]*North Carolina State University, Raleigh,* [2]*Universidade Federal de Pelotas,* [3]*University of Nebraska, Lincoln.*

The objective of this research was to identify QTL for growth and reproduction in female mice. Genotypic and phenotypic data were collected on 442 female progeny of *inter se* matings from an F_1 cross between line L6 (small BW) and line M16i (large BW), from two replications. Females were exposed to unrelated F_1 males B6C3F1/J until a copulatory plug was detected. BW were taken at 3, 6, 10 wk and at detection of the copulatory plug (PW); tail length was measured at 10 wk. Females were killed at d 16 of pregnancy to obtain counts on number of corpora lutea (TCL) and number of live (TF) and dead (TD) fetuses; embryo survival rates (ES) were calculated. Genotyping was done at 72 microsatellites in all F_2 females bearing a litter. Each of the 19 autosomes had at least three markers. A model with the effects of replication and litter within replication was fitted to the data. Residuals from this model were used in conjunction with a linkage map for the molecular markers in a composite interval mapping analysis. The putative QTL with largest additive effects ($P < .05$) on BW and tail length were found to be linked with markers in chromosomes (chr) 6, 8, 11, 12, 14, and 19. The major QTL for PW were found in chr 4, 5, 7, 11, 12, 14, and 18. QTL with additive effect on TCL were in chr 4, 11, and 14; significant associations between markers and putative QTL with additive effects were found in chr 9, 13, 14, 17, and 19 for TF and in chr 2, 4, 5, 6, 9, and 17 for TD. ES were affected mainly by QTL with additive effects linked to markers in chr 2, 9, 14, and 17. Putative QTL with the largest dominance effects ($P < .05$) were found for PW in chr 2 and 17, for BW in chr 10, 11, 12, and 17, for tail length in chr 6, 9, and 13, for TCL in chr 11, 17, and 18, for TF in chr 2 and 11, for TD in chr 9, and for ES in chr 2 and 11. There is definite indication of QTL for growth and reproduction. Some QTL may be pleiotropic due to detectable effects on several traits associated with the same markers.

Key Words: Mice, Quantitative Trait Loci, Growth, Reproduction

327 Comparison of approaches for determining significance threshold values for QTL detection. H. K. Lee*[1], J. C. M. Dekkers[2], M. Malek[2], M. Soller[3], R. L. Fernando[2], and M. F. Rothschild[2], [1]*National Livestock Research Institute, Korea,* [2]*Iowa State University, Ames,* [3]*Hebrew University of Jerusalem.*

Setting critical values (CV) for significance tests for detecting quantitative trait loci (QTL) with interval mapping is much debated. Several methods have been proposed to derive CV to control Type I error at the chromosome, experiment, or genome level, accounting for the number and dependence of tests, including the analytical method of Lander and Kruglyak (1995) (LK) and the permutation test (PT) of Churchill and Doerge (1994). Weller et al. (1998) proposed controlling false discovery rate (FDR) as basis for an alternative CV. The goal here was to compare 5% CV based on these 3 methods, recognizing that Type I error rate and FDR have different interpretations and relevance. Phenotypes of 5 meat quality traits and genotypes of 41 markers on 8 chromosomes covering 9.1 M (0.75 to 1.3 M per chromosome) from 525 F2's from a swine breed cross were used. Data were analyzed by least squares regression interval mapping with a test every cM. The PT CV were based on 10,000 replicates and FDR CV on tests at every cM. The 5% CV for a single test was 3.1. Experimentwise CV were 9.4 for LK and ranged from 7.1 to 7.4 for PT and from 4.4 to 6.7 for FDR, depending on the trait. Chromosomewise CV ranged from 6.5 to 7.2 for LK, from 4.6 to 5.2 for PT, and from 3.2 to 4.3 for FDR. Chromosomewise FDR behaved erratic due to dependence among tests and could not be obtained for several chromosome-trait combinations, for which FDR was above 5% for all tests, indicating no trait QTL on that chromosome. In conclusion, CV differed substantially between methods, leading to different numbers of QTL detected. FDR resulted in the least stringent CV. This while an FDR of 5% will be conservative for most purposes. This work was supported by an industry consortium of the National Pork Producers Council, Iowa Pork Producers Association, Iowa Purebred Swine Council, Babcock Swine, Danbred USA, DEKALB Swine Breeders, PIC, Seghersgenetics USA, and Shamrock Breeders.

Key Words: QTL Mapping, Significance Test, Breed Cross

328 Fitness of sheep metallothionein 1-a sheep growth hormone (oMt1a-oGH) transgenic mice. E. J. Eisen*[1] and J. D. Murray[2], [1]*North Carolina State University, Raleigh,* [2]*University of California, Davis.*

Objectives were to determine if the oMt1a-oGH transgene shows normal mendelian segregation and if oMt1a-oGH mice exhibit normal growth without the zinc supplementation required to increase plasma oGH levels and stimulate growth. Transgenic mice were reciprocally backcrossed for four generations to high growth and control lines to form lines GM and GR. In the fifth generation, hemizygous transgenic mice (T/-) were crossed within each line. Pooled across backcross generations, there was a deficit($P < .001$) of T/- progeny in GM (31.6%) and GR (22.2%) compared to expected (50%). In the T/- x T/- cross the combined percentage of homozygous (T/T) and hemizygous transgenic mice was less ($P < .001$) than expected (75%) in both GM (44.2%) and GR (38.5%). Backcross T/- mice had lower ($P < .05$) 3-wk body weights and lower ($P < .001$) 6-wk body weights and 3-6 wk postweaning gains than nontransgenic mice. Similar genotypic differences were found in the T/- x T/- cross. No significant growth differences were found between T/T and T/- progeny. Using segregation ratios from the T/- x T/- mating, the relative fitness estimate of T/T, T/- and -/- (nontransgenic) mice were .345, .223 and 1.0, respectively, in line GM and .218, .205 and 1.0 in line GR. Fitness estimates in the backcross for T/- and -/- were .463 and 1.0 in line GM and .285 and 1.0 in line GR. Abnormal segregation ratios may be due to germline mosaicism or reduced fitness due to differential embryo survival. Reduced growth of oMt1a-oGH transgenic mice when the transgene is switched off suggests a subtle developmental abnormality, which may contribute to a reduction in fitness.

Key Words: Transgene, Growth Hormone, Mice

329 Mutation in exon 5 of bovine prolactin gene is not associated with milk traits in Holstein bulls. I. Parmentier[1], N. Gengler[1], P. Laliberte[2], W. Holtmann[2], C. Bertozzi[1], V. Haezebroeck[1], D. Portetelle[1], and R. Renaville*[1], [1]*Gembloux Agricultural University, Gembloux, Canada,* [2]*Semex Alliance, Guelph, Canada.*

The prolactin hormone, PRL, plays a critical role in lactation. This hormone is, primarily responsible for the synthesis of milk proteins, lactose, and lipids, all major components of milk. In addition, PRL has been shown to directly stimulate insulin-like growth factor-I binding proteins, epidermal growth factor, a glycolysated mucin, parathyroid-like peptide, and PRL-inducible proteins in normal and neoplasmic tissue. The objectives of this research were to identify mutation in exon 5 of bovine PRL gene and to establish association between observed mutation and milk traits in Holstein bulls DNA was extracted from semen of 1100 Holtsein bulls provided by Semex-Alliance (Guelph, Canada). A mixed model was used to study association between alleles and milk, protein and fat yields. In this model, herd, year, season, parity, lactation, age classes, month of lactation were fixed effects and permanent environment, animal and residual effects were considered as random effects. Using BESS-Scan Mutation Detection and localization Kit (Epicentre Technologies), a mutation was found in the fifth exon of the PRL gene. By DNA sequencing, a A to G transition was identified at the 718 amino acid of the protein. In our population, allelic frequencies of the A and G alleles were 0.34 and 0.66, respectively. Statistical analysis showed no significant effect of PRL polymorphism at the exon 5 on lactation traits. In conclusion, the PRL polymorphism found in the fifth exon was not associated with lactation traits of Holtein bulls. This polymorphism is, thus, not a tool of choice for using in breeding programs. This research was supported by Belgian Ministery of Agriculture grant 5859 and Semex Alliance, Guelph, Canada.

Key Words: Prolactin, Mutation, Lactation

330 Genetic analysis of candidate gene (RELN) for Weaver Syndrome in Brown Swiss Cattle. S. E. Speidel*[1], E. Oberg[1], M. B. Abdallah[1], and S. K. DeNise[1], *University of Arizona, Tucson.*

Weaver Syndrome or Bovine Progressive Degenerative Myeloencephalopathy (PDME) is a recessively inherited neurological disease described in Brown Swiss Cattle that has been mapped to bovine chromosome 4 (BTA4). To locate the PDME causative gene, human and murine candidate loci have been identified that map to homologous regions on