Portal Development Research Report

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Project Title: Biological pathways associated with lactation performance

Award Date and Term: Awarded on May 9th 2011, for six months (~Nov 9th 2011)

Executive Summary:

Specific Objectives:
To identify biological pathways associated with lactation performance by comparing the mammary transcriptome expression profiles from CBA/CaH, QSi5 mice, and a CBAxQSi5 Advanced Intercross Line (AIL) during lactation and pregnancy.

1. We have established an Advanced Intercross Line (AIL) by back-crossing CBA/CaH and QSi5 mice for 14 generations. Our previous observations showed significant differences in lactation performance between these two inbred strains of mice, assessed by litter weight gain for the first 8 days of lactation (Ramanathan et al., 2008), while the lactation performance of AIL mice showed an intermediate phenotype (Ramanathan et al., 2007).
2. We collected mammary gland tissue from the pregnant CBA/CaH and QSi5 mice (on pregnancy day12; P12) and the lactating CBA/CaH, AIL and QSi5 mice (on lactation day 9; L9). Total RNA from the mammary tissue was purified and used for the Affymetrix Gene Chip assays (Affymetrix Mouse Genome 430 2)
3. Gene Set Enrichment Analysis (GSEA) of the microarray expression data of mammary gland from 10 pregnant mice (5 CBA/CaH and 5 QSi5 at pregnancy day 12) and 6 lactating mice (3 CBA/CaH and 3 QSi5 at lactation day 9) to identify the gene sets and the leading edge genes differentially expressed between mid-lactation and mid-pregnancy. (Supplemental file 1)
4. GSEA of the microarray expression data of mammary gland from 16 lactating mice (3 CBA/CaH, 3 QSi5 and 10 AIL) to identify the gene sets and leading edge genes highly correlated with pup weight gain. (Supplemental file 2)

5. Comparison of leading edge genes extracted from the pregnancy-lactation and lactation performance-correlation analyses to identify leading genes with the expression profiles that differentially expressed between pregnancy and lactation and also positively correlated with pup weight gain.
6. Leading edge genes with expression profiles satisfied both criteria were then analyzed using DAVID for functional annotation enrichment analysis. (Supplemental file 3)
7. Results from the DAVID analysis were then input to Enrichment Map ($P < 0.001$, $Q < 0.05$, Jaccard Overlap Combined Index (k constant = 0.5)) for visualization of the significant functional networks highly associated with lactation performance.(Figure 1 and Supplemental file4)

Significance and industry benefits

The functional networks and genes presented here have two important characteristics – 1) differentially expressed between lactation and pregnancy and 2) highly correlated with pup weight gain. The outcome provides valuable information about the gene networks and pathways involved in regulation of lactation performance. This work has implications for translating fundamental mammary gland biological data into milk production in dairy cattle.

References

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RAMANATHAN, P., MARTIN, I. C., GARDINER-GARDEN, M., THOMSON, P. C., TAYLOR, R. M., ORMANDY, C. J., MORAN, C. & WILLIAMSON, P. 2008. Transcriptome analysis identifies pathways associated with enhanced maternal performance in QSi5 mice. *BMC Genomics,* 9**,** 197.