273 Translating the physiology of fertility into improved phenotypes for genetic selection. M. Lucy*, University of Missouri, Columbia, MO.

In most dairy systems, the ability to establish pregnancy following insemination is the primary definition of fertility. Highly fertile cows establish pregnancy sooner after calving and require fewer inseminations. Pregnancy is a logical endpoint for defining the fertility phenotype because it is typically recorded on farm and can be verified by using calving dates. Pregnancy is established through a series of individual events that occur in sequence. In postpartum cows, for example, estrous cycles are re-established, estrus is expressed and detected, sperm are deposited in the reproductive tract and capacitate, ovulation occurs and is followed by fertilization, and the corpus luteum forms and produces sufficient progesterone to maintain pregnancy. The oviduct supports early cleavage and the uterus establishes a receptive environment for the developing pregnancy. Each individual event is theoretically heritable and these events collectively contribute to the phenotype of pregnancy after insemination. Genetic selection as it is practiced today does not target individual mechanisms leading to pregnancy because they are difficult to phenotype reliably on a large number of cows. Dairy systems differ with respect to reproductive management applied to cows. In some systems, cows are inseminated after detected estrus with minimal intervention. In these systems, the establishment of pregnancy early postpartum effectively captures the summation of the individual events leading to pregnancy. More intensive systems that use hormonal treatments (PGF$_{2\alpha}$, GnRH, etc.) followed by timed AI do not invalidate the current phenotypes but the individual components that contribute to the phenotype may be more or less important to the establishment of pregnancy. Uterine release of PGF$_{2\alpha}$ and the establishment of adequate circulating estradiol to cause an endogenous GnRH surge and estrus expression, for example, are not necessary to establish pregnancy when timed AI is used. Selecting cows for a functional reproductive system comprised of individual components involved in the establishment of pregnancy may ensure uniform performance of future cows across a variety of reproductive management systems.

Key Words: dairy cow, fertility, phenotype

274 The choice and collection of new relevant phenotypes for fertility selection. A. Fleming1, C. F. Baes1, F. Malchiodi1, L. F. Brito1, and F. Miglior*1,2, 1CGIL - University of Guelph, Guelph, ON, Canada, 2Canadian Dairy Network, Guelph, ON, Canada.

The fundamental aspect of dairying is successful reproduction. Impaired fertility represents a major financial loss for the dairy producer and is a prominent reason for involuntary culling. As selection for increased production was realized, deterioration in female fertility was witnessed, and, appropriately, selection indices expanded to include fertility traits, like calving interval, days open, calving to first service, first service to conception and 56d non return rate. The inclusion of fertility traits worldwide has had an impact in reversing the negative trend with regards to calving interval, days open and calving to first service, but little or no gain has been achieved for traits related to conception, such as first service to conception and 56d non-return rate. Fertility traits typically have low heritabilities, and relevant traits closer to the true reproductive biology are difficult to measure, making progress in female fertility challenging and the search for novel phenotypes appealing. Many alternative fertility indicator traits have emerged with the evolution of on- and off-farm technologies, such as milk progesterone and fatty acid profile, energy balance, and body weight and condition. The rise of genomic selection and genotyping breeding candidates becoming more commonplace may be particularly valuable for the improvement of fertility. The identification of novel lethal recessive genes affecting the viability of the pregnancy could aid in future matings. Haplotypes affecting fertility, including AH1 in Ayrshires, have already been described, and genomics may further uncover underlying genetic components influencing fertility for more effective selection. Reproductive technologies have alleviated some problems but perhaps only temporarily concealed the issue at hand. Genetic improvement of fertility of dairy cattle in the future will require more relevant phenotypes to be evaluated that more closely describe fertility, and those, which promote the improvement of fertility without intensive intervention from the producer.

Key Words: fertility, novel phenotype, trait identification

275 Embryonic survival: The other side of fertility—A genomic perspective. H. Khatib*, Department of Animal Sciences, University of Wisconsin, Madison, WI.

Currently within in vitro production systems, preimplantation mammalian embryos are selected for transfer to a recipient based on morphological assessment including visual valuation of cell number, fragmentation, compaction, and color for grading the embryo in terms of stage and quality. Though embryos may be of similar morphology, they may not be of similar developmental competence. Transcriptomic analysis performed in our laboratory revealed differential expression of 793 genes between in vitro- and in vivo-derived embryos, with 35 genes uniquely expressed within the in vivo embryos and 10 genes uniquely expressed within the in vitro embryos. A more efficient method of embryo selection would assess the potential reproductive success of both gametes and embryos based on their underlying genetic potential. miRNAs are a class of non-coding RNA that are 18–22 nucleotides in length which act to regulate gene expression of their target mRNAs through a RNA interference mechanism. These miRNAs have been found to be secreted out of cells into the extracellular environment with relatively high stability. Recently, we found that miRNAs are secreted by in vitro produced embryos into their respective culture media, and that these small RNAs are differentially expressed between conditioned media from embryos of differing development competence. We also fund that male and female embryos differentially secrete miRNAs via extracellular vesicles and that these secreted miRNAs serve as signals to the mother. Implications from these studies set the framework for future development of method for non-invasively surveying the developmental potential of embryos based on miRNA biomarkers.

Key Words: pregnancy, fertility, energy balance, and body weight and condition.
The objective of this study was to investigate if loci associated with pregnancy at first service were shared with loci associated with pregnancy at ≥4 services in Holstein heifers and cows. Nine hundred 2 heifers and 1032 primiparous cows were bred by artificial insemination during observed estrus for up to 5 consecutive estrus cycles for heifers and up to 13 cycles for cows. Pregnancy was determined via palpation on d 35 for heifers and cows not returning to estrus. Heifers and cows were genotyped using the Illumina BovineHD BeadChip (777,962 SNPs) and a genome-wide association study (GWAS) was conducted with a significance threshold of $P < 5 \times 10^{-8}$ to identify individual associations and $P < 1 \times 10^{-5}$ to identify shared associations. The GWAS identified 65 SNPs associated with pregnancy to first service in heifers and 138 SNPs associated with pregnancy to first service in cows. Eleven SNPs associated with pregnancy to first service were shared among heifers and cows. One hundred 64 SNPs were associated with the number of times bred (1, 4 or 5 times) required for pregnancy at d 35 in heifers, 79 SNPs were associated with times bred (1, 4–13 times) in cows and 7 SNPs were shared among Holstein heifers and cows. Two loci were associated with all phenotypes in heifers and cows. These results indicate that although most loci associated with pregnancy per artificial insemination in heifers and primiparous cows are unique, there are shared loci that are important in achieving pregnancy in both groups that could be used for genomic selection. This project was supported by Agriculture and Food Research Initiative Competitive Grant no. 2013-68004-20365 and 2018-67015-27577 from the USDA National Institute of Food and Agriculture.

Key Words: genome-wide association study (GWAS), dairy heifer, loci

277 Big data genomic investigation of dairy fertility and related traits with imputed sequences of 27K Holstein bulls. J. Jiang1, P. VanRaden2, J. Cole2, Y. Da3, and L. Ma*1, 1University of Maryland, College Park, MD, 2Animal Genomics and Improvement Laboratory, Beltsville, MD, 3University of Minnesota, St Paul, MN.

Imputation has been routinely applied to ascertain sequence variants in large genotyped populations based on reference populations of sequenced animals. With the implementation of the 1000 Bull Genomes Project and increasing numbers of animals sequenced, fine-mapping of causal variants is becoming feasible for complex traits in cattle. Using the 1000 Bull Genomes data, we imputed 3 million selected sequence variants to 27,000 Holstein bulls after quality control edits and LD pruning. These bulls were selected to have highly reliable breeding values (PTAs) for 35 production, reproduction, and body conformation traits. We first performed whole-genome single-marker scan for the 35 traits using the mixed-model based association test in MMAP (https://mmmap.github.io). The single-locus association statistics were then merged in multi-locus analyses of 3 groups of traits, production, reproduction, and body conformation, respectively. Candidate genomic regions 2 Mb long, were selected based on the multi-locus analyses and used in fine-mapping studies. We implemented a state-of-the-art fine-mapping procedure with a Bayesian method that can assign a posterior probability of causality to each variant and for each independent association signal generate a minimum set of associated variants whose total posterior probability of causality exceeds a threshold (e.g., 95%). Our fine-mapping identified 36 candidate genes for production traits, 48 for reproduction traits, and 29 for body conformation traits, respectively, including some previously reported causal variants, e.g., Chr6:38027010 in ABCG2 for production traits and Chr7:93244933 in ARRDC3 for reproduction and body conformation traits. The candidate variant list may facilitate follow-up functional validation and expand our understanding of complex traits in dairy cattle. Additionally, our method can be readily applied to other species where large-scale sequence genotypes are available.

Key Words: genomics, reproduction, dairy

278 Genetic cues from fertilization to pregnancy establishment. M. S. Ortega*1, J. B. Cole2, T. E. Spencer1, and P. J. Hansen3, 1University of Missouri, Columbia, MO, 2Animal Genomics and Improvement Laboratory, ARS, USDA, Beltsville, MD, 3University of Florida, Gainesville, FL.

One approach to improve genetic selection for reproductive traits is to identify SNP in genes linked to reproductive processes. Genes in which these SNP reside represent targets for physiological intervention to improve fertility. Sixty-eight SNP previously associated with genetic merit for fertility and production were tested for association with daughter pregnancy rate (DPR) and other fertility traits in an independent population of Holsteins. There were 22 SNP in genes associated with genotypic estimates of fertility in the 2 Holstein populations; moreover, animals carrying allelic variants associated with higher genetic merit for fertility also exhibit more favorable phenotypic measurements of fertility. DPR reflects days open, which entails many physiological events including the ovulation of a competent oocyte, adequate sperm transport in the reproductive tract, successful fertilization in the oviduct, and development and implantation in the uterus. Genes containing SNP repeatedly associated with reproductive traits provides an indication of physiological processes important for variation among cows in reproductive function. Among the genes associated with fertility traits in both populations 14 genes were regulated by steroids, there were also genes involved in processes including oocyte quality (COQ9), fertilization (BSP3), trophectoderm formation (WBP1), and lipid biosynthesis (ACAT2, HSD17B7, and HSD17B12). Future directions should include functional studies involving genome engineering to understand the biological role of genetic variants in the tight regulation of reproductive function in cattle.

Key Words: fertility, embryonic development, pregnancy establishment