GENOMIC SELECTION FOR IMPROVED FERTILITY OF DAIRY COWS WITH EMPHASIS ON CYCLICITY AND PREGNANCY

I.1. Introduction

The **overall objective** of this integrated proposal that includes **research, extension, and education components** is to make use of advanced genomic technologies to improve the efficiency of dairy animals for fertility traits through genomic selection contributing to the long term sustainability of food systems, enhancing the United States and the global food security.

To achieve this objective, our aim is to identify single nucleotide polymorphisms and haplotypes associated with direct measures of dairy cow fertility and reproductive efficiency in dairy populations, and subsequently develop comprehensive extension and education programs that deliver science-based information to an extensive audience. It is our **central hypothesis** that reproduction in dairy cows is controlled, to some extent, by genetic components and sufficient genetic variation for fertility traits exists in cattle populations to implement efficient selection programs. The **long term goal** of this multistate project is to provide new resources for the understanding, and consequently, the improvement of dairy cattle fertility via identification of **molecular markers significantly** associated with reproductive efficiency.

I.1. Specific Objectives

Objective 1: Develop a fertility database with genotypes and phenotypes based on objective and direct measures of fertility in lactating dairy cows.

Sub-Objective 1.A.: Assess fertility phenotypes evaluating direct measures of fertility (puerperal uterine health, resumption of postpartum ovulation, expression of estrus, pregnancy per insemination, and maintenance of pregnancy) in a large population of lactating dairy cows (n = 12,000) under different management practices and environments, representing dairy cattle populations of 4 regions of the U.S. (Northeast, Midwest, Southeast, and Southwest).

Sub-Objective 1.B.: Collect and store DNA and detailed productive, reproductive and health related information from this population (n = 12,000) to create a database publically available for future research.

Sub-Objective 1.C.: Develop and validate a reproductive index as an estimator of fertility in this population of lactating dairy cows. The individual scores from the reproductive index will be used as a continuous variable for the selection of two extreme high and low fertility populations.

Sub-Objective 1.D.: Select two subpopulations of lactating dairy cows representing extremes for high (n = 850) and low (n = 1,750) fertility to be submitted for genotyping. The classification of cows will be based on the reproductive index score.

Sub-Objective 1.E.: Perform genotype determination (SNPs and copy number variation [CNV]) in the selected high and low fertility subpopulations (n = 2,600) by use of a high-density DNA analysis platform.

Objective 2: Identify SNPs and haplotypes significantly associated with fertility traits by use of genome-wide analyses to build a base for genomic selection of dairy cows for improved fertility.

Sub-objective 2.A.: Perform genome-wide association studies (GWAS) to detect polymorphisms markedly contributing to variation of each fertility trait considered, including potential pleiotropic effects.

Sub-objective 2.B.: Develop genomic selection models utilizing selected sub-sets of SNPs with superior predictive ability of genetic merit for reproductive efficiency, using cross validation approaches.

Sub-objective 2.C.: Validate the genomic prediction models in two populations: 1) an independent pool (n = 1,000) of cows selected from the entire population; 2) a group of A.I. sires with extreme values for fertility (DPR; 200 sires).

Sub-objective 2.D.: Apply SNP-based gene-set enrichment analysis (GSEA-SNP) to identify candidate genes based on SNP associations resulting from the GWAS.

Objective 3: Develop best selection practices and economics for AI studs and for on-farm use of genetic markers for improved fertility and overall productivity of dairy herds.

Sub-Objective 3.A.: Develop best selection practices based on their return on investment that could be easily implemented by AI studs and applied by dairy farmers. Expected long term products include genomic breeding values for puerperal uterine health, resumption of postpartum ovulation, expression of estrus, pregnancy per insemination, and maintenance of pregnancy.

Sub-Objective 3.B.: To develop a web based self-evaluation program for farm reproduction and genetics practices.

Objective 4: To develop and assess a comprehensive scientific-research based extension programming on best management and genomic selection practices to improve fertility in dairy herds.

Sub-Objective 4.A.: To deliver the relevant findings of this study through extension road shows and the eXtension system including DAIReXNET as a collaborator of this project. The goal will be to utilize traditional extension methods and the latest in Internet technologies to speed the delivery of novel approaches for improving fertility by use of genomic tools to dairy farmers as well as to place that information into the broadest context.

Sub-Objective 4.B.: Evaluate changes in the understanding and subsequent use of genomic tools for genetic selection for improved fertility over time in response to the research and extension developed in this project using producer focus groups and data collected from individual dairies and DHIA.

Sub-Objective 4.C.: To make available our relevant findings to the USDA-ARS Animal Improvement Programs Laboratory and to A.I. companies to incorporate fertility breeding values into the national genetic improvement program for US dairy cattle and to facilitate a timely translation of our results into commercial tools that could be incorporated into the routine farm management.

Objective 5: Train and mentor undergraduate and graduate students enrolled in Master and Doctoral programs and develop a course module to be included in the Dairy Institutes presented every summer in NY and NM and make these materials public and available on a web based tutorial at the partner universities of this project (dairy extension programs in FL, IL, MN, NY, TX, WI).

Sub-Objective 5.A.: Expose undergraduate students to research activities to stimulate interest towards graduate school and food animal oriented careers. Incorporate students pursuing Master and Doctoral degrees in the different areas involved in the project, including reproduction and management of dairy cows, bioinformatics, and genetic selection in dairy cattle.

Sub-Objective 5.B.: To develop and deliver a comprehensive educational course module that addresses key traditional and genomic selection practices for the dairy industry to teach Animal Science and Veterinary students from multiple Universities attending to the Dairy Summer Institutes hosted at Cornell (NY) and to the Southern Great Plains Dairy Consortium Summer Teaching Institute presented at Clovis (NM). Additionally, this module will be available on a web based tutorial at the partner universities of this project (TX, FL, MN, Cornell, OH, WI, IL) for integration in formal student education and potential nationwide use in distant learning programs.

Sub-Objective 5.C.: Evaluate changes in the overall knowledge and skills in students attending to the summer institutes (Cornell and NM) with emphasis on genetic/genomic selection for improved fertility and reproduction in dairy cattle.