Southeast Dairy Producer's Check-Off Program

Research Summary

Discovery of genetic markers linked to protection of cells from elevated body temperature

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Funding Year: 2023 **Amount Awarded:** $20,000

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Methods

A long-term goal is to give producers the tools to produce a dairy cow that is genetically resistant to heat stress and that still maintains the capacity for high milk yield. It is known that there is genetic variation among cows in how heat stress affects body temperature and milk yield. Much of this work was supported by the Milk Checkoff Program. Among the takeaways from this research is that it is possible to select cows for resistance to heat stress but that doing so could also lead to lower milk yield. This is because cows that produce more milk also produce more metabolic heat and are therefore more sensitive to heat stress. One strategy for selecting for thermotolerance without also reducing milk yield is to select for genes that protect cows from heat stress independent of those causing reduced milk yield. Recent research indicates that genes involved in protection of cells from elevated temperature are involved in thermotolerance. Selecting for these genes should improve thermotolerance; many of these genes are unlikely to have a negative effect on milk production. The goal of the proposed research is to identify genetic markers for genes protecting cells from elevated temperature. If successful, these markers could be incorporated into genomic tests for thermotolerance. The approach we are taking is to collect white blood cells from cows that have been genotyped with the Clarifide Plus genotyping chip from Zoetis and evaluate survival of the cells after exposure to elevated temperature. Earlier, we showed that there are breed differences in the degree to which white blood cells undergo a type of cell death called apoptosis. A statistical procedure called genome-wide association study (GWAS) will be performed to identify genetic markers that explain variation in the degree to which white blood cells are killed through apoptosis by elevated temperature. The study will be performed on a cooperating dairy farm in which cows are enrolled in the Zoetis Clarifide Plus program. Each week, blood samples will be collected from up to 50 cows in mid-gestation via tail vein. Samples will be collected from pregnant cows to reduce possible variation due to reproductive status. Blood samples will only be collected in cool months to avoid confounding effects of heat stress. Data on individual cows such as parity, stage of lactation, and milk yield will be collected so that data can be adjusted to remove these effects. The total number of cows to be sampled will be 1600. Blood samples will be centrifuged to collect the buffy coat containing white blood cells. White blood cells will be cultured in an incubator for 24 hours at either 101.3°F (normal body temperature of the cow) or 105.8°F (characteristic of body temperature during severe heat stress). At the end of the culture period, cells

will be labeled for apoptotic cell death using the In Situ Cell Death Detection Kit (Roche Diagnostics, Indianapolis, IN). For each cow, cell survival will be calculated as the increase in percent dead cells caused by elevated temperature. Subsequently, genomic information will be retrieved from the Council for Dairy Cattle Breeding and GWAS will be performed to identify genetic markers for cell survival. The specific program used for this analysis will be the ssGBLUP procedure.

Results

Key to a successful outcome of this research will be developing an assay that allows us to measure disruption of cell function by heat stress on large numbers of cows. The assay must be easy to implement and not very expensive. Currently, we have been working on optimizing such an assay. The original approach has been to measure cell death in response to elevated temperature using flow cytometry. In initial studies, white blood cells have been shown to be largely resistant to killing by elevated temperature. Thus, we are looking for new assays that we can use (for example function of mitochondria) so we can screen cows for cellular resistance to heat stress.

The work continues - we expect to develop a suitable assay and complete the objectives of the proposal.