THESIS

EVALUATION OF POPULATION GENETIC STRUCTURE IN TWO BRITISH *Bos taurus* BREEDS ACROSS FIVE U.S. CLIMATE ZONES

Submitted by

Bethany Cornwell Krehbiel

Department of Animal Sciences

In partial fulfillment of the requirements

For the Degree of Master of Science

Colorado State University

Fort Collins, Colorado

Spring 2017

Master's Committee:

Advisor: Milton G. Thomas

Harvey D. Blackburn
R. Mark Enns
Scott Speidel
Patrick Byrne

ABSTRACT

EVALUATION OF POPULATION GENETIC STRUCTURE IN TWO BRITISH *Bos taurus* BREEDS ACROSS FIVE U.S. CLIMATE ZONES

The objective of this thesis was to determine the fine-scale genetic diversity in Hereford and Red Angus cattle in relation to climate. Two hundred and twenty-five Hereford cattle and 174 Red Angus prominent AI sires were assigned to five U.S. climate regions (Cool Arid, Cool Humid, Transition Zone, Warm Arid, and Warm Humid). SNP-based methods were used to evaluate genetic diversity in the cattle in each of the U.S. climate zones. The first method utilized neutral SNP and the ADMIXTURE software to determine the genetic structure of the population. The second method used 66 SNP associated with traits potentially influenced by climate (body weight, heat stress, milk yield, heifer conception rate, and early embryonic survival) to determine Hardy-Weinberg Equilibrium and detection of loci under selection in each climate zone for Hereford and Red Angus breeds. Using 14,312 SNP, analyses of Hereford cattle revealed genetic structure that corresponded with climate zone. Additionally, 15 of the 66 SNP violated Hardy-Weinberg Equilibrium and detection of loci under selection ($P < 0.05$). Analysis of the 15 SNP revealed allele frequencies that were unique to the climate zones. Using 13,960 SNP, the genetic structure analysis of Red Angus sires revealed that there were eight sub-populations present within the breed. Additionally, 23 of the 66 SNP violated Hardy-Weinberg Equilibrium and detection of loci under selection ($P < 0.05$). Allele frequency analysis of the 23 SNP did not show genetic substructure that corresponded to climate zone. In conclusion, fine-scale evaluation of Hereford cattle revealed a genetic substructure corresponded with climate zone. However, fine-scale genetic substructure was detected in Red Angus sires, but did not correspond to

U.S. climate zones. By identifying the genetic diversity in these prominent British beef breeds in relation to climate, management strategies can be formed to utilize the genetic diversity of these breeds to combat climate change.

ACKNOWLEDGMENTS

First, I would like to acknowledge Dr. Milt Thomas and Dr. Harvey Blackburn for their unending support, education, and patience as I have grown as an animal scientist. Without their guidance as advisors, I would not be where I am today in my career. In addition, I would like to acknowledge my committee members Dr. Scott Speidel, Dr. Mark Enns, and Dr. Pat Byrne for their guidance throughout my Master's program.

Thank you to my co-workers Carrie Wilson, Dr. Danielle Paiva, Dr. Samuel Paiva, Dr. Phil Purdy, and Scott Spiller at the USDA-ARS-National Animal Germplasm Program for supporting my efforts and giving me new and fresh ideas to consider in my research. Thank you for the time you've spent with me as friends and as leaders. Your stories and opinions have meant a lot to me.

Finally, thank you to my fellow graduate students, friends, and family for allowing me to voice my ideas, frustrations, and successes with you. To my fellow graduate students, you guys have become my closest friends, and I hope we continuously educate and enjoy each other throughout our careers. To my family, thank you for your support and love throughout my journey.

DEDICATION

I would like to dedicate this thesis to my family and my husband, Scott. They have supported me in every way, and nurtured my passion for agriculture.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1: INTRODUCTION

Introduction

Climate change has the potential to dramatically alter cattle productivity throughout the world. Global warming is expected to increase drought, reduce forage and crop production, and decrease livestock production due to decreased reproductive performance, metabolic efficiency, and altered immune response (Nardone et al., 2010). In order to respond to the negative impacts of global warming, selection of animals that prosper in diverse environments is necessary to maintain or improve production, such as milk, meat, or fiber. Animals that can produce in diverse conditions are those that are composed of genetically diverse genotypes which allow for environmental adaptation (Booy et al., 2000).

Mutation, genetic drift, and natural selection help to increase genetic diversity within a population (Slatkin, 1987), but according to Booy et al. (2000), genetic variation must be present within a local population to allow adaptive differentiation between populations. With the occurrence of gene by environment interactions (G x E), maintaining genetic diversity throughout a population may be needed in order to sustain cattle production in differing climate environments.

Recently, development of genomic technology enabled identification of the adaptive ability of animals through molecular markers, which are associated with quantitative trait loci (QTL; Booy et al., 2000; Hayward et al., 2015). A review of literature of this topic reveals that climate change in conjunction with G x E interaction can be measured through allele frequency of loci potentially influenced by climate. The objective of this thesis was to determine if SNP-based genetic substructure was present

within two *Bos taurus* breeds across five U.S. climate zones. Genetic structure could be identified and used to determine the genetic diversity of cattle that can be used in combatting climate changes.

CHAPTER 2: LITERATURE REVIEW

Bovidae Bos taurus

History

Artiodactyla, also known as even-toed ungulates, have inhabited the world since approximately 1000 AD. Today's most populous domesticated ungulates include *Bos taurus and indicus* (cattle), *Ovis aries* (sheep), and *Sus scrofa* (pig). Cattle, also known as *Bos taurus* (humpless) or *Bos indicus* (humped), were separated into two different lineages more than 200,000 years ago from separate domestications (Mctavish and Hillis, 2013) and domesticated approximately 10,000 years ago (Daetwyler et al., 2014). Through the evolution of ungulates, many anatomical characteristics can be attributed to their ancestors and the adaptation that has occurred over time, such as horn type, dentition, and skeletal confirmation (Prothero and Foss, 2007). Many current characteristics of these livestock production animals can also be attributed to their selection for milk, meat, fiber, or draft power.

Bovidae is a diverse herbivore family that inhabits many areas of the world. Due to this, environment has driven natural selection (compared to artificial selection) within this family (Prothero and Foss, 2007). For example, indicine animals are highly tolerant to tropical environments. They have slick hair, a humped neck, pendulous ears, loose skin, and well-developed sweat glands to facilitate heat tolerance. Each of these features in the *Bos indicus* animals enables the body to draw heat away from the internal organs and dissipate through the skin. Conversely, taurine animals do not contain these features, but vary in body size, carcass quality, milking ability, and muscularity due to their use as draft animals, milk animals, and (or) difference in

terrains in which they were derived. Hammond et al. (1996) and Cartwright et al. (1955) reported that *Bos indicus* cattle (i.e., Brahman) are more tolerant to heat stress than *Bos taurus* cattle (i.e., Hereford). For example, both studies showed that when put under artificial heat stress, the body temperature of Brahman cattle was at least one degree cooler than the Hereford cattle (°F). Additionally, the heart rate was notably different, with Brahman cattle having 28 beats per minute (bpm) less than Hereford cattle as reported in Hammond et al. (1996), and Brahman cattle having 51.7 bpm less than Hereford as reported in Cartwright et al. (1955). Although indicine cattle are biologically more suitable to warmer environments, there has been evidence of tropically adapted *Bos taurus* breeds such as Tuli, Senepol, and Romosinuano (Cundiff et al., 2012).

Indicine and taurine animals are the major cattle species that currently inhabit the United States. Originally from India, *Bos indicus* cattle are the most populous cattle in the world. Although these cattle breeds (e.g., Brahman) are associated with heat tolerance, they are typically lighter muscled and slower growing than most *Bos taurus* breeds (Hammond et al., 1996). *Bos taurus* cattle derived from the Fertile Crescent and are classified as British (i.e. England, Scotland origin) or Continental (i.e., France, Germany origin) breeds. British cattle are associated with moderate frame size, early maturity, and mothering-ability. Continental cattle typically have a large frame size and are associated with growth and carcass traits. However, market forces have caused British and Continental breeds to change significantly. For example, recent observations have revealed similar weaning weights, yearling weights, and maternal milk between British and Continental breeds (Kuehn and Thallman, 2012).

British Breeds

British *Bos taurus* breeds include, but are not limited to, Hereford and Red Angus cattle. Hereford cattle originated in Herefordshire, England. According to the American Hereford Association (2016), this breed was developed due to the expanding meat market created by Britain's Industrial Revolution. In 1817, Kentucky statesman Henry Clay brought Hereford cattle to the U.S., and the American Hereford Association was formalized in 1881 (AHA, 2016). The present-day Hereford is known for its hardiness, early-maturity, and docility (AHA, 2016).

Red Angus cattle originated in Northern Scotland and were brought to the U.S. in the 1870s. The breed was originally called Aberdeen Angus and there was no distinction between the recessive red and dominant black coat colors of this breed (RAAA, 2016). Black Angus cattle can, however, produce Red Angus offspring if both sire and dam contain the recessive red coat color allele. George Grant transported four black Angus bulls to Victoria, Kansas in 1873. At that time, Angus cattle were different from many of the breeds in the U.S. because they were polled. The American Aberdeen Angus Association was established in 1883. In 1917, the association preferred the black coat color to represent the Angus breed, and barred the registration of all other colors of cattle (RAAA, 2016). Subsequently, the Red Angus Association of America was established in 1954. Though originally not genetically distinct, the Red Angus and Black Angus breed associations considered themselves distinctly different in the United States.

Selection Trends

In the 1950s, beef cattle were selected for compact size and generous fat deposition (Willham, 1982). This led to an extreme change of selection towards smaller cattle across the beef cattle industry in the U.S. When beef packers paid less for fat cattle (AHA, 2016), production of cattle shifted to large frame-sized cattle, with moderate fat deposition. Expected Progeny Differences (EPDs) were first published in the late 1970s (Golden et al., 2009). This allowed breeders to compare animals, select for economically relevant traits, and make improvements of the breeds. Specifically, EPDs are calculated using phenotypic records of related animals to produce a value that reflects a breeding animal's genetic merit. Technologies such as artificial insemination (AI), embryo transfer, sire evaluation, and pedigree analysis enabled breeders to select for animals that fit the industry's needs. For example, since the inception of EPDs in the 1970s, weaning weight, yearling weight, and milk have steadily increased in Red Angus and Hereford breeds. However, in both Hereford and Red Angus breeds, birth weight EPDs marginally increased, and has remained relatively constant compared to other growth trait EPDs (RAAA, 2016; AHA, 2016).

Currently, Hereford and Red Angus cattle have the second and fourth most registered beef cattle in the U.S., respectively (RAAA 2016, AHA 2016). The American Hereford Association has consistently registered about 65,000 to 75,000 cattle per year in the last decade, where the Red Angus Association of America has steadily increased its registration counts to approximately 50,000 (RAAA, 2016; AHA, 2016). Additionally, Hereford and Red Angus cattle are heavily utilized in composite breeds such as Beefmaster, Red Brangus, Braford, Stabilizer, as well as commercial programs that

cross Hereford cattle on Black Angus to produce what is commonly called a black baldy (Mason, 1969).

Because of the utilization of multiple breeds in a breeding program, the Roman L. Hruska Meat Animal Research Center (USMARC) in Clay Center, NE developed an adjustment factor that allowed EPDs from across breeds to be compared (Van Vleck et al., 2007; Kuehn et al., 2010). The across-breed EPDs method was introduced in the late 1980s and is updated annually. Without the across-breed EPDs, comparison of EPDs would not be accurate because EPDs are computed separately for each breed. Black Angus serves as the basis in which all other breed EPDs are adjusted. The adjustment factors are useful in comparing EPDs, but cannot be used to directly compare breeds.

Compared to Black Angus, Hereford and Red Angus cattle required 2.3 and 2.5 EPD adjustments for birth weight, respectively. Hereford cattle required a weaning weight EPD adjustment of -7.8, whereas Red Angus cattle required a -31.4 EPD adjustment. Hereford and Red Angus cattle required approximately a -30 yearling weight EPD adjustment compared to Black Angus. For milk, Hereford cattle required a much larger EPD adjustment at -17.7 where Red Angus cattle only required a 3.3 EPD adjustment (BIF, 2016).

Bovine Genome

The first bovine DNA sequence was published in 2009 (Elsik et al. 2009) and cost $53 million (Zhou et al., 2015). The highly inbred Hereford Line 1 Dominette cow was the first bovine sequenced due to its high homozygosity. The University of Maryland (UMD3.1) and Baylor College of Medicine Human Genome Sequence Center

(Btau4.6) sequence assembled Dominette; however, the assemblies were not in concordance with each other. In short, two different algorithms were used by the entities to assemble the genome. There were discordances between the two methods, which led to the production of BtOM1.

The BtOM1.0, also known as the bovine optical map, was designed to resolve the disparities of UMD3.1 and Btau4.6. BtOM1.0 utilized iterative and *de novo* methods in order to accurately assemble the bovine genome sequences. The iterative process required a reference genome, in which the UMD3.1 was chosen due to its more accurate assembly in comparison to Btau4.6 (Zhou et al., 2015). The iterative process used the reference sequence to attach to Rmaps, which are the restriction maps of a single genomic DNA molecule. Next, overlapping bins were formed from the Rmap piles, which were then independently assembled into optical contigs. Lastly, the assembled contigs become the updated reference for eight cycles of alignment and assembly (Zhou et al., 2015).

The *de novo* assembly is used when the previous method contains uncontiged Rmaps. This method utilized de Bruijn graphs and “seed maps,” which were produced from Rmaps that were connected to each of the highly confident nodes in the graph (Zhou et al., 2015). Compared to the BtOM1.0 versus UMD3.1 and Btau4.6, results revealed 7,463 discordances for Btau4.6, and 4,754 for UMD3.1 (Zhou et al., 2015). Ultimately, BtOM1.0’s combined iterative and *de novo* processes forms a more complete assembly, where discordances between previous methods are resolved and contigs are fully recovered.

Genomic Selection

The use of genomic selection has been an increasingly utilized practice in the beef industry since Meuwissen et al. (2001) estimated the effects of approximately 50,000 marker haplotypes associated with phenotypic records. Traditionally, selection practices were based upon phenotypic measurements of an individual and successively incorporated phenotypic measurements of that animal's relatives to form an estimated breeding value (Meuwissen, 2016). With advances in molecular genetics, genotypes were used to gain more information about the genes underlying economically relevant traits (ERT). Molecular markers, such as amplified fragment length polymorphisms, restriction fragment length polymorphisms, variable number of tandem repeats (microsatellites) and single-nucleotide polymorphisms (SNP) have been utilized to identify relationships between genotypes and phenotypes. The marker-assisted selection (MAS) method utilized these markers to identify genes that were significant for an effect on a trait. However, gross QTL detection made it difficult to estimate breeding values because of the numerous genes that underlie these large chromosomal regions. Some of these effects were too small to be statistically significant, and therefore, were ignored (Meuwissen, 2016). Additionally, MAS requires prior knowledge of a population. For example, MAS is applicable to known associations to specific traits of interest. Because of this, only known alleles or markers with quantitative estimates can be utilized and therefore selected only in families (Eggen, 2012).

Genomic selection assumes that all markers are potentially linked to a gene that subsequently affects a trait (Meuwissen, 2016). Because SNP are numerous (e.g. ~100 million; Kitts and Sherry, 2002) and widespread throughout the bovine genome, they

may be associated with genes that ultimately influence a trait. Genomic breeding values assess genetic potential of a breeding animal based upon the summed effects of a SNP on a trait (Bagnato and Rosati, 2014). Genomic breeding values are produced through the use of training and validation data. The SNP effects are estimated from trained data, which is a conglomerate of phenotypic, pedigree, and molecular information. With this information, the known phenotypes are regressed on the SNP and its effects are estimated (Akdemir, 2014). Subsequently, the genomic breeding values of new animals are predicted, based upon the estimated SNP effects in the reference, or trained population. This is called the validation data, which is only comprised of genotypes. Genomic selection does not require the prior knowledge of alleles or marker positions due to its full use of the genome in estimating and predicting genomic breeding values (Eggen, 2012).

Matukumalli et al. (2009) used sequence information to develop a high density SNP genotyping assay that would scan the bovine genome for variation. The BovineSNP50 assay contains 54,001 SNP that are evenly spaced across the bovine genome. The median inter-marker interval distribution of the BovineSNP50 is 37 kb, with a maximum predicted gap of 350 kb (Matukumalli et al., 2009). Genome-wide association studies (GWAS) have utilized the BovineSNP50 BeadChip because of its "simultaneous high-throughput interrogation of hundreds of thousands of loci with high measurement precision at an affordable cost," (Matukumalli et al., 2009).

To further improve genetic evaluation in beef cattle, Kuehn et al. (2011) analyzed genotypes of more than 2,000 prominent AI sires using 54,001 markers included on the BovineSNP50 BeadChip. The 2,000 Bull Project determined the relationships between

genomic variation and economically relevant traits, in addition to breed composition, and less quantified traits such as feed efficiency and disease resistance. This project involved U.S. breed associations (n=16) with the greatest number of registrations and included the Angus, Hereford, Simmental, Red Angus, Gelbvieh, Limousin, Charolais, Shorthorn, Brangus, Beefmaster, Maine-Anjou, Brahman, Chiangus, Santa Gertrudis, Salers, and Braunvieh breeds (Kuehn et al. 2011).

By studying prominent AI sires with the greatest influence on the industry, more information regarding genomic variation in relation to economically relevant traits can be obtained from the sires' progeny. Also, using the 54,001 SNP markers, the 2,000 Bull Project aided industry with issues such as lack of pedigree information, disease traceability, or G x E interactions. In addition, predicting heterosis or breed effects could be determined with knowledge of high density SNP and allele frequencies in a population (Kuehn et al., 2011).

Daetwyler et al. (2014) whole-genome sequenced 234 key ancestors of Jersey, Fleckvieh, and Holstein-Friesian bulls to determine sequence variants associated with health and welfare traits. This study was the first phase of the 1,000 Bull Genomes project, which aimed to construct a whole genome sequence database of key ancestors of modern cattle breeds (Daetwyler et al., 2014). This study identified 28.3 million sequence variants within the three cattle breeds. These variants were comprised of 1.6 million indels (insertion deletions) and 26.7 million SNP. Eighty percent of the variants identified were novel.

From these novel variants, Daetwyler et al. (2014) investigated mutations that potentially affected fertility in the three dairy breeds. A recessive mutation underlying

embryonic death was detected on chromosome 2 at position 94,410,507. This mutation occurred at the structural maintenance of chromosome 2 (SMC2) and substitutes a thymine for a cytosine in the DNA sequence. This results in an amino acid replacement of a phenylalanine by a serine, and has been reported in other species to cause embryonic lethality (Daetwyler et al., 2014).

Additionally, a dominant mutation underlying lethal chondrodysplasia was detected. This mutation results in a calf with disproportionate dwarfism, including: short neck, swollen cranium, and reduced body and limb length (Daetwyler et al., 2014; Agerholm et al., 2004). Because the affected cattle were heterozygous at the syndrome's locus, Daetwyler at al. (2014) hypothesized the disease was a dominant mutation and mosaicism occurred in the sire germ line. Mosaicism occurs when cells within one individual contain more than one genotype. Of the effected animals, there were two candidate mutations, including one mutation that affected the COL2A1 gene. This mutation occurred on chromosome 5 at position 32,475,732, where a guanine allele was substituted for an adenine allele in the DNA sequence. This substitution was predicted to replace a glycine with arginine in the amino acid sequence. According to Daetwyler et al. (2014), the COL2A1 mutation was also reported to negatively affect human skeletal structure. After further analysis in affected animals, Daetwyler et al. (2014) showed a strong association between the mutation and the disorder.

By determining the sequence variants within Jersey, Fleckvieh, and Holstein-Friesian cattle, the 1,000 Bull Genomes project provided a database that is utilized to determine health and wellbeing traits in these breeds. Additionally, by utilizing these genotypes in whole-genome wide association studies, Daetwyler et al. (2014) imputed

sequences to determine variants associated with milk yield and curly coat. The 1,000 Bull Genomes project was able to identify relevant variants that producers can utilize to make informed decisions about animals to keep or cull within their production system.

With advanced technologies in molecular genetics leading to genomic selection, molecular markers have taken on a more extensive role pertaining to the bovine genome. Difficult to measure traits such as fertility, feed efficiency, or longevity, can be studied and breeding values estimated. Furthermore, these advanced methods are used to determine the effects of climate-mediated pressure on an animal's genome. Selection signatures, which are loci under natural or artificial selection, can be statistically associated with climate factors. Genomic selection has allowed the identification of the selection signatures in addition to aiding in producer selection when considering climate adaptability and difficult to measure traits in their breeding objective. "Genomics leads to a more objective view of genetic value of animals that is not limited to a few production traits" (Eggen, 2012).

Phenotype to Phylogenomics

Before the use of genome-enhanced EPDs, selection methods such as tandem selection, selection index, and independent culling levels were used to select for desired traits (Hazel and Lush, 1942). Tandem selection allowed producers to put emphasis on one trait until it was improved, then select for another trait until it was improved, etc. the selection index method allowed producers to select for multiple traits simultaneously by using a net merit index. The independent culling levels method required the animals to reach a certain desired level in each specified trait, and if not, be culled from the herd (Hazel and Lush, 1942). Although the producer selected desired levels of the traits

within his or her herd, the animal that won in the show ring influenced selection (Willham, 1982; Madalena, 2005). Therefore, much of the selection that represented the ideal animal was based upon phenotype. Until the introduction of EPDs, the progress in understanding economically relevant traits was relatively slow. With EPDs, the compilation of many phenotypic and pedigree records in many different herds within the same breed could be utilized to improve and select for superior animals.

Since the bovine genome was sequenced, genomic information on livestock has aided selection in many ways. For example, genetic abnormalities can be identified in affected animals using DNA testing. This led to widespread genomic testing of cattle for diseases such as arthrogryposis multiplex (curly calf), tibial hemimelia, pulmonary hypoplasia with anasarca and many more. Additionally, with genome sequencing, new tools such as genomic-enhanced EPD and genomic selection have been utilized to increase the accuracy and scope of selection while decreasing generation interval (Lôbo et al., 2011; Garcia-Ruiz et al., 2016).

Now, genotyping domestic *Bos taurus* or *Bos indicus* is very common. High-density genotyping has been highly successful in gaining knowledge on genotype to phenotype associations (Nishimura et al., 2012; Weng et al., 2016). Additionally, the bovine genome has been used to gain information on ancient ancestral populations to accurately determine the line of descent of a species and gain more information on today's breeds (Hanotte et al., 2000; Delsuc et al., 2005; and Decker et al., 2009). This method of genomic research is called phylogenomics, which incorporates information of segment homology with the strategies of evolutionary cladistics (O'Brien and Stanyon, 1999). Once homologous pieces are identified (i.e. amino acids, genes, morphological

structures, ultrastructural characteristics of cells, biochemical pathways, or nucleotides) phylogenetic inference methods such as distance, maximum parsimony, and likelihood methods can be used to reconstruct evolutionary history of a species. The principles can be divided into sequence-based methods and methods that are based on whole-genome features (Delsuc et al., 2005).

The distance method compares all pairs of sequences and estimates an evolutionary distance. Next, these distances are used to generate a tree in which the patterns and lengths represent the distance matrix and relationship from one species to another (Eisen, 1998). The maximum parsimony method compares potential phylogenomic trees and selects the tree that requires the least number of character changes that would be required over evolutionary time to fit the sequences into that tree (Eisen, 1998; Delsuc et al., 2005). The maximum parsimony test identifies genome arrangements. Genome arrangements are an indication that adaptation occurred and potentially facilitated species formation (O'Brien and Stanyon, 1999). Because genome arrangements are rare and easily identifiable, they are informational evolutionary characteristics to analyze. Lastly, the likelihood method constructs trees and selects the optimal tree based on the likelihood the given sequence would have evolved into a particular tree given a model of amino acid or nucleotide substitution probabilities (Eisen, 1998).

Knowledge of ancestral origins of current cattle populations can give insight to conservation opportunities, breed formation, and history of domestication (Decker et al., 2009; Moritz, 1995). Using interspecific molecular phylogenies, inferences can be made about populations and their course of development over time. Moritz (1995) asserted

that through phylogenomics, individual lineages contributing to the genetic diversity within a clade could be determined. Decker et al. (2009) performed a high-throughput phylogenomic study that determined the genotypes of ancient, extinct Pecoran DNA.

Phylogenomic studies have served as a supplement to phylogeny studies, where previous phylogeny studies have relied mostly on morphological and ultrastructural character to construct lineages. For example, through skeletal conformation, dentition, horn type, ruminant/non-ruminant status, it has been determined that *Bos taurus* are related to *Bos indicus* animals, which are both related to *Ovis canadensis* (Bighorn sheep). Though they are not similar in appearance, they are all ruminants, even-toed ungulates, and monophyletic. However, phylogenomic studies can further assess a species genomically, where molecular characters may give more insight to the true origin or composition of a species. Kuehn et al. (2014) demonstrated this through a genomic assessment of 16 U.S. cattle beef breeds. Specifically, *Bos taurus* cattle contain the same characteristics and are derived from aurochs (*Bos taurus primigenius*). However, it has been shown phylogenomically that *Bos taurus* breeds Red Angus and Hereford are at opposing ends of the phylogenetic tree, demonstrating the dissimilarity in genetic base of two breeds (Kuehn et al., 2014). Therefore, it would be advantageous to determine the differences in these breeds and how to best utilize those differences in production systems today.

Climate Change

According to the Intergovernmental Panel on Climate Change (2014), each of the last three decades has been successively warmer at the earth's surface than any preceding decade since 1850. This warming has led to increased sea levels, increased

ocean acidification, decreased glacier mass, and decreased precipitation in some areas, consequently affecting global regions dissimilarly (IPCC, 2014).

Anthropogenic greenhouse gas emissions increase the concentration of carbon dioxide, methane, and nitrous oxide in the earth's atmosphere. Human activity has had a large effect on greenhouse gas emissions due to population size, energy use, and land use patterns. Greenhouse gas emissions have been detected throughout the globe and have largely contributed to climate changes since the mid-20th century (IPCC, 2014). The IPCC (2014) asserted that more frequent hot and fewer cold temperature extremes over most land areas on daily and seasonal timescales will occur as global mean surface temperature increase due to greenhouse gas emissions. These events will also manifest longer and more frequent heat waves (IPCC, 2014).

In addition to increased greenhouse gas emissions and the earth's warming, water quality and availability for animals is a major concern as global warming progresses. Nardone et al. (2010) reported that water salination is spreading in many areas of the world. Furthermore, water pollutants such as chemical contaminants, heavy metal concentration, biological contaminants, and altered pH could adversely affect livestock, especially during increased thermal events when water intake increases (Nardone et al., 2010). Water quality and quantity are vital to beef production, considering the global average water footprint of meat from cattle is 15,400 liter/kg (Mekonnen and Hoekstra, 2010).

Climate change affects animal production in numerous ways; the change in climate has the potential to alter the quality and amount of forage available, in addition to affecting the animals through heat stress (Adams et al., 1998). Livestock have a

thermoneutral zone in which they are not under climatic stress. When livestock experience warm climatic events and exceed their thermoneutral zone, heat stress occurs and adverse effects on production are possible, such as decreases in milk yield, reproduction, and feed intake (Holter et al., 1997; West, 2003; Bohmanova et al., 2007; and Collier et al., 2009).

To measure thermal stress on livestock, an index representing combined effects of temperature and humidity has been formulated (THI; Bohmanova et al., 2007). This allows producers to monitor livestock stress in relation to heat. Efforts to avert climatic stress such as fans, mists, and shade, have been explored, but these works are mostly applicable to confinement operations (Mader, 2003).

Weather fluctuations also have adverse effects on animals. Senft and Rittenhouse (1985) analyzed cattle responses to temperature stress in free-range and feedlot settings. Within each feed setting, feed intake in relation to acclimation period and behavioral responses in relation to short-term thermal stress were measured. Feed settings had a significant effect on the behavioral response to short-term thermal stress, whereas length of physiological acclimation period to environment (as measured in feed intake) varied for the breeds used in this study (i.e. Polled Hereford, Hereford, Angus, and Santa Gertrudis). Thus, results suggest not only do extreme thermal events adversely affect cattle production, but fluctuation in temperatures may also be detrimental to cattle production efficiency.

With the occurrence of severe weather changes all species are liable to extinction if not genetically equipped with sufficient diversity, robustness, or plasticity. Manel and Holderegger (2013) reported that population decline is directly linked to the

loss of intraspecific genetic diversity. Furthermore, Boettcher et al. (2015) stated diverse animal genetic resources allows for more opportunities to combat severe climatic events influencing populations. Den Boer et al. (1993) demonstrated how diversity is vital to combatting environmental changes in insects. Carabid *Pterostichus oblongopunctatus*, a type of ground beetle, was able to achieve adaptability to wet and dry forest conditions because of its genotypic variation across the population. A diverse genetic foundation enabled the beetle to tolerate differing moisture conditions, and allowed the beetles to occupy a wide range of forests and avoid extinction (Den Boer et al., 1993).

In addition to genetic diversity, breeding for general robustness or plasticity may also provide opportunity to allow animals to survive in dissimilar climates. As defined by de Jong and Bijma (2002), plasticity is the animal's ability to display different phenotypes in various environments. Conversely, robustness shows less phenotypic variability in various environments. Breeding for robustness and plasticity in livestock populations is possible if a breeding objective is for health and welfare traits (Star et al., 2007). As international swine and poultry layer industries are expected to perform in hotter and more intensive conditions, robust animals that balance production and fitness-related traits are needed in order to continue production (Knap, 2005). Napel et al. (2009) suggested multi-trait selection, heterosis, and natural selection all provide ways in which animals can become more robust and less prone to environmental stress. Furthermore, Napel et al. (2009) and Knap (2005) suggested the use of genetic correlations and DNA markers in association with the environment to accurately select genotypes that produce in diverse climates.

Sufficient diversity, robustness, and plasticity all provide ways in which animals can cope with extreme weather conditions, but Notter (1999) and Paaby and Rockman (2014) suggested that lowly productive stocks might also be useful in adapting to climate change. Through cryptic gene variation, livestock may exhibit phenotypic variation when under abnormal conditions, such as extreme climate events (Paaby and Rockman, 2014). Gibson and Dworkin (2004) defined cryptic gene variation as genetic variation that does not contribute to the normal range of phenotypes observed, but is displayed when the animal responds to perturbation within its environment. While cryptic gene variation is expressed under extreme environments and may provide opportunity to adapt to climate conditions, further research to detect, manage, and determine the extent of its effects is necessary in order to take advantage of this potential hidden variance.

It is vital for producers to have access to a wide range of genotypes in production systems that are easily influenced by the environment. As livestock industries such as poultry, swine, and dairy cattle are increasingly standardized, the loss of interbreed genetic diversity increases (Notter, 1999). In the past 50 years, the poultry industry has undergone extreme changes and confinement systems now produce more than 40 billion birds annually (Muir et al. 2008). This has led to significant absences of rare alleles in commercial poultry breeds. Muir et al. (2008) stated that genetic diversity within the poultry industry has been reduced because of the limited breed utilization and within-line selection. The reduction of diversity may potentially serve as a major issue in commercial chicken lines where disease outbreak and climate change could hinder

production. Alternative production systems may need to be investigated to cope with future industry needs.

With continual climate change and the suspected increase of the human population size to 9 billion by 2050 (Lutz and KC, 2010) food security will be of high priority. The need for adaptable animals is imperative, especially for nations with impoverished people, who depend on animals for their livelihood (Thornton et al., 2009). Moreover, climate change will severely affect developing countries and their socioeconomic issues (Fischer et al., 2005). Socioeconomics analyzes the relationships between societies and other economies. Agriculture is the predominant source of income in most developing countries (Parry et al., 2001). Because all facets of agriculture are directly or indirectly dependent on climate, the livelihood of people affected the most by climate change may need to change in order to preserve food security and provide income-generating options (Jones and Thornton, 2009). By producing and selecting adaptable or robust animals, the negative effects of climate change could be alleviated and provide a more stable food supply contributing to long-term economic prosperity. In addition to socioeconomic threats, millions of people are at risk from future climate change in developing countries because of water shortage, hunger, coastal flooding, and malaria. According to Parry et al. (2001), by 2080, 3.5 billion people will be susceptible to these hazards.

It is evident that the need for adaptable animals is vital to sustainability as climates continue to change. Fussel (2007) stated two societal responses to reduce the risks of climate change are mitigation and adaptation. Although these approaches combat climate change differently, they are complementary. Mitigation decreases the

amount of greenhouse gas emissions whereas adaptation responds accordingly to the climate. Mulder et al. (2006) raised the question whether the world can be supplied with one optimum global genotype, or if specialized genotypes for each environment are required to continue production. For now, by identifying adaptive animals, livestock producers can exploit opportunities for improvements, which can ultimately be used to address issues such as water shortage, increased temperatures, and decreased forage.

Gene by Environment Interaction

Because of severe climatic changes throughout many areas of the world, gene by environment interaction (G x E) is important as producers seek to find the ideal genotypes of animals that are able to produce in various climate conditions. Genotype by environment interaction occurs when there are differences in expression of genotypes between environments (Cromie et al., 1999). Measuring the G x E within populations is difficult, considering the differences in production systems, phenotypic records, and accuracy of records. In addition, animals must be subjected to diverse environments to obtain observations. Bowman (1972) stated that the comparison of measurements between two or more environments may not necessarily be the same due to the difference in gene expression in dissimilar environments, providing more challenges to measuring G X E. Genotype by environment interaction has made it challenging to identify relevant QTL associated with economically relevant traits. For example, Long et al. (2008) and Ye et al. (2006) illustrated the changes in appropriate SNP associated with mortality and other performance traits in poultry based upon dissimilar hygiene environments.

Although G x E may be difficult to analyze, it is present, has varying effects on animal agriculture, and has been observed in domesticated and feral populations (Burns et al., 1979; Robinson et al. 2009). A series of G x E studies were conducted from 1961 to 1974 that evaluated production traits from two different lines of Hereford cattle that resided in contrasting environments of Florida and Montana (Burns et al., 1979, Butts et al., 1971, Koger et al., 1979, and Pahnish et al., 1983). Burns et al., (1979) evaluated birth and weaning measurements of Florida and Montana derived Hereford cattle in each location of the cattle's development. The Montana line averaged 10 kilograms heavier weaning weights in Montana, but in Florida, the Montana line averaged 9 kilograms lighter weaning weights than Florida line cattle. Additionally, Koger et al., (1979) evaluated reproductive traits of these two different lines. A line by location interaction was observed for pregnancy and weaning rates. Results also revealed an advantage of the local population in comparison to the introduced lines. The difference in performance between these two lines of cattle revealed a clear G x E interaction, which illustrates the importance of adaptation to a specific environment for beef cattle production.

Reproductive technologies have allowed dispersion of genetics in many environments across the world. Through AI, bulls can be used in a variety of production systems. Within the dairy industry, Zwald et al. 2003 and Raffrenato et al. 2002 showed how dairy bulls rank differently based upon the climate environment in which they are utilized. In other instances, feral animals have adapted to their environment, which has shaped their development and ability to survive (Robinson et al., 2009). For example, Chirikof Island, AK cattle have showed signs of adaptation to environment. These

unmanaged cattle were secluded on an island in the North Pacific Ocean and survived for generations as feral livestock (McKnight, 1964). Chirikof Island cattle are in existence because of human migration and the animals accompanying them. In fact, using the BovineSNP50 BeadChip, Decker et al. (2016) showed that Chirikof Island cattle are related to a variety of breeds including Russian Yakut, Hereford, Holstein and Angus. The integration of these bloodlines resulted in a unique and differentiated gene pool in comparison to other contemporary North American cattle breeds (MacNeil et al., 2007; Decker et al., 2016). Their gene pool, combined with climate, shaped a cold-adapted, hardy breed that survives in the Alaskan climate.

Livestock have shown signs of adaptation to their corresponding environment. However, the study of genetic associations between traits in relation to environment has been less studied. Robinson et al. (2009) evaluated associations between sexually dimorphic traits horn length, body weight, and parasite load in feral Soay sheep, whom reside on the island of Hirta, St. Kilda in the northwestern region of Scotland. These traits were evaluated between and within sexes and across differing environments. This unmanaged population has been on the island since the Bronze Age, and has served as a study population since 1985. Results indicated that the genetic correlations between the three traits changed based on climate. For example, Robinson et al. (2009) reported that horn length was genetically correlated with body weight in males, but not females. Furthermore, environmental conditions the Soay sheep experienced during childhood influenced the genetic correlation among traits within and between the sexes. Based from these results, Robinson et al. (2009) suggested evolutionary processes may largely depend upon ecological conditions.

Gene by environment interaction can be used as an advantage for livestock producers. It would be advantageous to embrace G x E through identification and selection of those animals that have proven consistent production in their climate residence or shown signs of adaptation phenotypically or molecularly. Genomic selection could aid in selecting accurate markers such as SNP or QTL when considering environmental factors for improving production.

F-Statistics

In study of the subject of population genetics, Sewall Wright defined multiple measurements that explained genetic structure in populations. One of the most widely used measurements is the inbreeding coefficient, which Wright (1950) defined as "the departure from the amount of homozygosis under random mating toward complete homozygosis" (Wright, 1922a). It can also be defined as the correlation of uniting gametes, represented as *F* (Wright, 1950). Three measurements derived from *F* were used to further identify the genetic structure of a population. The *F*-statistics, (also known as fixation indices), F_{IS}, F_{IT}, and F_{ST}, represents total population (T), subdivisions (S), and individuals (I; Wright, 1965). Specifically, F_{IT} is the correlation of uniting gametes to produce individuals, in relation to gametes of that population (Wright, 1965). F_{IS} is the correlation between uniting games of the average overall subdivisions in relation to those gametes of their own subdivision. Lastly, F_{ST} is the correlation between random gametes within their subdivisions. This correlation is relative to the gametes of the total population (Wright, 1965). The *F*-statistics identify genetic structure within populations. However, the fixation indices can be influenced by level of inbreeding, genetic drift, mutation, artificial selection, or natural selection.

Selection Signatures

Livestock animals undergo selection pressures, either artificially or naturally. Genetic change brought on by selection pressure is reflected in changes to the animal's genome. Although there are many factors that are responsible for genetic diversity including genetic recombination, mutation, sexual reproduction, etc., other causes such as climate can induce natural selection of particular alleles that allows an animal to survive in certain environments. Amplified fragment length polymorphisms, restricted fragment length polymorphisms, and microsatellites have been used to assess the genetic variation of populations and individuals. However, recently, selection signatures have been used to quantify differentiation in the genome through statistical approaches that identify reduced local variability, specific linkage disequilibrium patterns, and deviated spectrum of allele frequencies (Kim and Nielsen, 2004). Selection signatures provide an alternative method to identify genetic differentiation among populations, in addition to identifying regions of the genome influenced by climate.

Gutiérrez-Gil et al. (2015) described selection signatures as regions of the genome that contain functionally important sequence polymorphisms that are selected through natural or artificial selection, leaving distinct patterns of DNA behind. Kim and Nielsen (2004) asserted that when beneficial mutations are continuously selected, extreme changes in spatial distribution, linkage disequilibrium, and the frequency spectrum might occur at the site where the mutation took place, therefore, providing a genomic region in which selection signatures may be identified. To identify signs of selection within the genome, several statistical methods are utilized (Kreitman, 2000; Jooste et al., 2007). According to Sabeti et al. (2006), all statistical tests to detect

positive selection are based broadly on five signatures: high proportion of function-altering mutations, reduction in genetic diversity, high-frequency derived alleles, differences between populations, and long haplotypes.

When mutations occur, they may serve no functional effect on the population, or they can be deleterious and harm the fitness of the population. Consequently, the allele frequency of that mutation does not increase nor become fixed (Sabeti et al., 2006). However, when favorable alleles are selected for a prolonged period of time, the allele frequency for that functional variant increases and may become fixed (Sabeti et al., 2006). Detection methods analyze the high proportion of function-altering mutations in comparison to other populations to detect positive selection through their allele frequencies.

Selection signatures can also be identified through reduction in diversity. When a region is under selection, unique genomic patterns are left behind. These patterns include the hitchhiking effect (i.e. linkage disequilibrium), which consists of neutral areas of loci downstream or upstream of the functional variant (Kim and Nielsen, 2004). Figure 1 illustrates loci under selection in addition to the linked alleles associated with the selected loci. The region that has undergone selection is called a selective sweep. Reduction in diversity occurs through selective sweeps where the loci not under selection are linked to the loci under positive selection leading to the elimination of diversity within this region (Sabeti et al., 2006; Charlesworth, 2007)

The third method of detecting selection signatures is through high-frequency derived alleles. According to Sabeti et al. (2006) high-frequency derived alleles are nonancestral alleles that arise through mutation. Usually, derived alleles have lower

allele frequencies than alleles inherited from their ancestors. However, derived alleles will increase in frequency if they are linked with a favorable allele that is positively selected. A region that contains many high-frequency derived alleles forms a selection signature that can be detected.

Selection signatures can also be identified through differences in allele frequencies in differing populations. When populations are subjected to different pressures such as climate or different breeding objectives, positive selection could change the frequency in one population but not another (Sabeti et al., 2006).

Lastly, long haplotypes are used to identify selection signatures. When positive selection occurs, some alleles increase relatively fast where genetic recombination does not occur. The alleles inherited with the selected allele forms a long-range haplotype. These are not typical, considering the long range haplotype would have a high frequency and long-range association with other alleles. This selective sweep forms an identifiable selection signature (Sabeti et al., 2006).

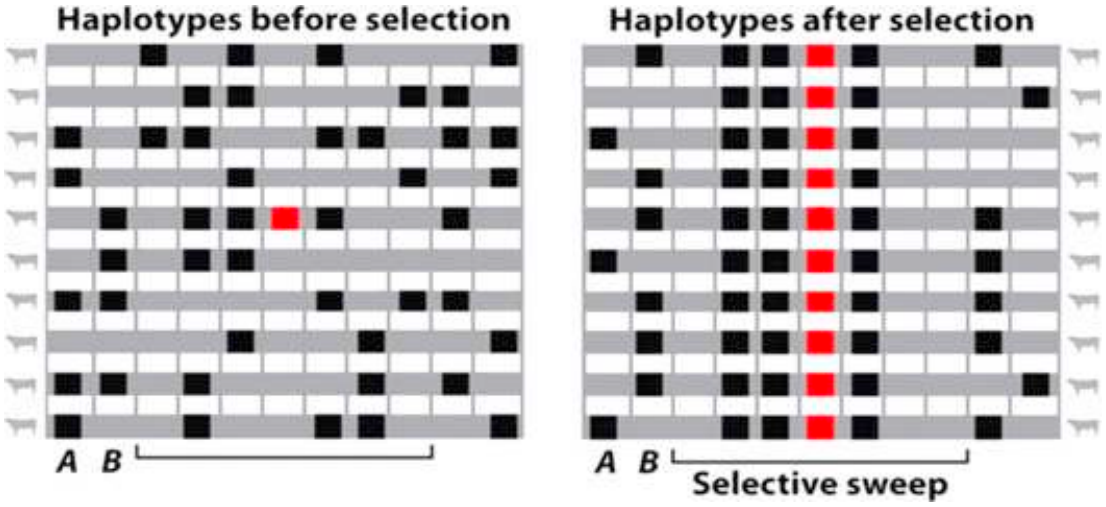

Figure 1. An illustration of loci under selection. The red loci represents a selected mutation, whereas the black loci represent the allele linked to the selected red loci (Qanbari and Simianer, 2014)

The detection of positive allelic selection throughout the genome is challenging. Although genetic footprints are utilized to identify areas under selection, subtle changes within the genome such as mutation, back mutation, strength of selection, recombination rate, and the type of selection all provide ways in which selection signatures can be influenced (Kreitman, 2000; Braverman et al., 1995; Kim and Stephan, 2002; Charlesworth, 2007; McVean, 2007). For these reasons, multiple methods of detecting selected loci are applied to connect genotypic to phenotypic variation.

The methods proposed for detecting selected loci can be classified based upon approach of selection signature identification and intra- or inter-population analyses (Harris and Meyer, 2006; Kreitman, 2000). By evaluating genomes within a population, local variability will be reduced (Qanbari and Simianer, 2014). Intra-population methods can then compare the difference between individuals of that population to the relative average across the genome. Inter-population analyses utilize single site differentiation to determine selection signatures (Qanbari and Simianer, 2014). With inter-populations, genetic drift is assumed to affect all neutral loci similarly (Cavalli-Sforza, 1966). When selection occurs with one or more loci, the genomic regions surrounding the loci under selection will display increased F_{st} values (Wright's fixation index), which is a widely used value to determine the expected level of heterozygosity in a natural population (Wright, 1951).

As Fig.1 illustrated, when selection occurs, linked alleles may be selected because of their location near the selected loci. Tests based upon linkage disequilibrium (LD) can identify these selective sweeps. According to Kim and Nielson (2004) and

McVean (2007) these tests tend to be impermanent once fixation occurs because recombination quickly breaks down the LD.

Linkage disequilibrium tests are considered intra-population tests where the level of DNA polymorphism is assessed for a genome-wide set of loci within a population (Qanbari and Simianer, 2014). Tests associated with LD include long-range haplotype tests, (Sabeti et al., 2002), extended haplotype homozygosity, integrated haplotype score, (Voight et al., 2006), and haplotype allelic classes, (Hussin et al., 2010). Haplotypes are groups of alleles on a chromosome that are inherited together from a single parent (Balding et al., 2006). Haplotypes aid in LD tests where allele frequencies of the haplotypes may indicate a selection sweep. Linkage disequilibrium can be calculated using D', linkage disequilibrium or gametic disequilibrium, and r^2, Pearson's coefficient of correlation (Lewontin, 1988). These two measurements can determine whether alleles are or are not randomly associated with one another.

Gametic disequilibrium, D', measures the haplotype frequency in relation to the product of their corresponding allele frequencies. For example, given p_1 and p_2 = frequency of the alleles at SNP1 and q_1 and q_2 = frequency of the alleles at SNP2, then p_{11}, p_{12}, p_{21}, and p_{22} are the haplotype frequencies (Lewontin,1988; Risch, 1995). When haplotype frequencies are equal to the product of their corresponding allele frequencies (i.e. $p_{11} = p_1q_1$), then the loci are in linkage equilibrium. Conversely, if the haplotype frequencies do not equal the product of their corresponding allele frequencies, they are not in linkage equilibrium. Therefore, linkage can be calculated with the equation $D = p_{11}p_{22}-p_{12}p_{21}$. However, this value must be standardized because depending on the allele frequency of the loci, D can be negative, but actual gametic frequencies cannot be

negative (Lewontin,1988; Risch, 1995). Therefore, D' is used in the equation D' = D/Dmax, where Dmax = min (p_1q_1,p_2q_2) when D < 0, and Dmax = min (p_1q_2,p_2q_1) when D > 0. Pearson's correlation coefficient is calculated by using the equation $r^2 = ((D/\sqrt{(p_1p_2q_1q_2)}))^2$. A X^2 test can be used to determine significance of the D' and r^2 tests. Complete LD occurs when D' = 1 or $r^2 = 1$.

Although intra-population tests are based upon LD, they include additional standards to identify selection signatures. For example, long range haplotype tests utilize a core haplotype (SNP within a region so small recombination does not occur) in relation to SNP surrounding the core haplotype. The haplotype homozygosity is measured in a region in comparison to the frequency of the haplotype in the population, (Qanbari and Simianer, 2014). Subsequently, extended haplotype homozygosity tests measure LD at increasing distances from the core haplotype to evaluate decay of LD according to distance (Gouveia et al., 2014). Pan et al. (2013) applied the extended haplotype homozygosity technique to determine significant core regions in Chinese Holstein cattle. These significant regions identified important functional genes that pertained to milk production traits, which could help detect functional candidate genes under positive selection for further breeding research in Chinese Holstein cattle (Pan et al, 2013). Furthermore, integrated haplotype score is a continuation of extended haplotype homozygosity tests, which compares the homozygosity between derived and ancestral alleles within a population (Voight, 2006).

Inter-population tests evaluate population differentiation. Because populations are typically not under the same environmental or management conditions, positive selection pressures may change allele frequencies in one population but not in another

because of selection pressures or genetic drift. Wright's fixation index (F_{st}) is widely used to determine population differentiation. This inter-population test estimates the elevated F_{st} from multiple loci and compares these values with its neutral expectations to identify selection (Gianola et al., 2010). For this test, large varying F_{st} values signify selection whereas small heterogeneity signifies no selection (Gouveia et al., 2014). Unlike intra-specific tests such as long range haplotype and extended haplotype homozygosity, F_{st} tests identify actual genetic variants under selection because it is SNP-specific (Gouveia et al., 2014).

Recently, dairy cattle breeds were subjected to intense artificial selection towards improvement of milk production traits. Flori et al. (2009) utilized the F_{st} test to identify physiological pathways and regions, which were affected by selection in three French dairy breeds. Ultimately, by using the F_{st} test, Flori et al. (2009) was able to describe the antagonistic relationships between milk production and reproductive traits at the genome level.

Although intra- or inter-population tests reveal regions that have undergone selection within the genome through departure from neutrality, each test contains caveats when identifying genome differentiation. For example, detection methods lose statistical power once a specific selected allele reaches fixation (Gouveia et al., 2014). Detection methods such as F_{st} may encounter issues with population structure and the assumption of estimating variance of F_{st} under neutrality (Gouveia et al., 2014). Kreitman (2000) described the bias of detection methods lies within misinterpretation of statistical results because of the lack of independence, and suggests an empirical investigation in simulated data sets. Sabeti et al. (2006) suggested that selection

signatures can be influenced by population demographic history, such as genetic bottlenecks, expansions, and subdivided populations, which all may lead to incorrect identification of signatures.

Landscape Genetics

Identification of adaptive variation may provide opportunity to produce a robust animal that is suited for multiple environments. Traditionally, population genetics methods have been used to evaluate the fine-scale genetic structure within a population potentially due to artificial or natural selection, genetic drift, gene flow, etc. Recently, a landscape genetics approach, which integrates the effect of landscapes on evolutionary processes (Manel and Holderegger, 2013), has been utilized to determine how landscapes contribute to shaping a population's genome. Storfer et al. (2007) defined landscape genetics as "research that explicitly quantifies the effects of landscape composition, configuration, and matrix quality on gene flow and spatial genetic variation." Landscape genetics is unique as it combines population genetics, which is focused on evolutionary processes, with landscape ecology, which is focused on recent time periods, also known as microevolution (Montgelard et al., 2012).

Infrastructure, climate, and natural topographical barriers all play roles in landscape genetics and influence a population via its movement and spatial distribution across landscapes (Holderegger and Wagner, 2008). Though these factors may act as a hindrance to populations, the fragmentation of habitats may also aid in genetic variation across species due to diverse selection pressures in each individual's environment (Shoville et al., 2012).

According to Manel et al. (2003) landscape genetics studies examine the relationships between genetic and environmental variation at an individual level without defining populations in advance. Statistical tools are then used to determine the spatial genetic patterns, which are used to test for correlations of individuals to environmental variables (Manel et al. 2003). In addition to addressing population structure, fragmentation, connectivity, and identification of barriers, landscape genetics provides an approach to investigate genetic conservation. Inferences about the landscape features driving gene flow, or locally adapted animals allows the application of a spatial statistical analysis which would be informative to determine what are driving these factors (Segelbacher et al., 2010). Determining genetic fragmentation or population status can aid in conservation management practices or identification of diverse genotypes able to combat climate change (Segelbacher et al., 2010).

To capture the genetic variation in populations due to climate-induced adaptability, statistical intra-population and inter-population tests can be used to give insight of environment-driven genotypes. The associations made between climate variables such as temperature, humidity, sunlight, and precipitation and alleles could potentially provide evidence of SNP that have been under selection due to climate pressures.

United States Geography and Climate

The U.S. is a leading exporter of grain crops like corn, wheat, and sorghum (UN Comtrade, 2015). This is due to its unique abundance of loam and changing seasons, which can generate warm and cool season crops. Subsequently, the U.S. is divided into biomes due to the differences in climates and plants, which allows a variety of animals

to thrive in each of these environments. Wladimir Köppen produced the first climate classification map of the US in 1900. Since its inception, Rudolf Geiger updated the map in 1961 (Kottek et al., 2006). Most recently, Peel et al. (2007) updated the map that classified regions based on climate zones, precipitation zones, and temperature zones.

The United States is comprised of main climate zones described as climate, precipitation, and temperature including: Cfa (warm temperature, fully humid, hot summer); BSk (arid, steppe, cold arid); Csb (warm temperature, summer dry, warm summer); BWk (arid, desert, cold arid); Dfa (cold, fully humid, hot summer); BWh (arid, desert, hot); and Dsb (cold, summer dry, warm summer; Peel et al., 2007). Furthermore, the conterminous U.S. has been divided among ecological regions. Omernik and Griffith (2014) refined U.S. ecological regions based on levels, where Level I is the most generalized measurement of U.S. climate zones, and Level IV is the finest-scale measurement of U.S. climate zones. Ecological classification Level II represents approximately 21 Eco regions, with 6 main regions that largely cover the majority of the US including: West-Central, semi-arid prairies; South-central, semi-arid prairies; Southeastern USA plains; Ozark, Ouachita-Appalachian forests; Cold deserts; and Western Cordillera.

The climate and ecological classifications give insight into how the U.S. can be divided based upon environmental factors. With the previously mentioned climate and ecological regions considered, this thesis broadly utilized five climate zones within the U.S. that were coded as: Cool Arid (CA), Cool Humid (CH), Transition Zone (TZ), Warm Arid (WA), and Warm Humid (WH). The climate zones represent the vast environmental differences within the U.S.

CHAPTER 3: GENETIC SUBSTRUCTURE OF HEREFORD CATTLE IN FIVE U.S. CLIMATE ZONES[1]

Introduction

Climate change can induce gene by environmental interactions in animals, affecting production levels (Burns et al., 1979). A beef cow's ability to withstand climate impacts and continue production is imperative for her to stay in the herd and not be culled due to low production levels or reproductive failure. Although matching cow biological type to environment can improve production, a genomic evaluation is potentially more precise in selecting animals that produce in varying environments.

While current genetic selection procedures include genotyping animals to improve the accuracy of genetic predictions, environmental challenges and lack of genetic diversity could hinder these processes. Genome-wide association studies have revealed single-nucleotide polymorphisms (SNP) associated with traits affected by environment such as milk production (Lillehammer et al., 2008; Hayes et al., 2009) health, and fertility (Dikmen et al, 2013). Gaining knowledge of allele frequencies of genotypes potentially influenced by climate would give insight to how climate may be shaping the bovine genome in diverse environments. Therefore, selection practices may require modification to improve or maintain productivity within harsh climate zones.

The objective of this research was to perform a fine-scale genetic structure analysis of Hereford cattle distributed across U.S. geographic zones using two SNP panels: 14,312 neutral SNP and 66 SNP associated with traits potentially responsive to climate. The hypothesis of this research was that Hereford cattle residing in five U.S.

[1] Derived from a study produced by the author for the USDA-ARS. No copyright claim is made to the materials produced by the USDA-ARS.

climate zones contain a SNP-based genetic substructure influenced by climate. Through evaluation of SNP allele frequencies of Hereford cattle in each climate zone, the genetic variability within cattle populations can be assessed and potentially serve as a mechanism of adaptation to climatic change.

Materials and Methods

Cattle evaluated and genotyping

Data from 577 Hereford cattle were acquired from USMARC (i.e. 2,000 Bull Project), USDA-ARS-National Animal Germplasm Program (USDA-ARS-NAGP), and Sul Ross State University (SRSU), which had been genotyped with either BovineSNP50 BeadChip (54,001; Matukumalli et al., 2009) or BovineSNPHD BeadChip (777,962; Illumina Inc. CA). These data contained cattle of birth years 1953 to 2008, representing approximately 10 generations (i.e. average generation interval of 5 years). The 577 Hereford cattle were derived from 150 breeders representing 31 states in the U.S. Four hundred and ninety-one samples were from the 2,000 Bull Project (Kuehn et al., 2011). One-hundred and eighty of these sires had Line 1 influence in their pedigree, a highly inbred subpopulation of Hereford cattle (Leesburg, 2012). Eighty-six additional Hereford cattle, genotyped with BovineSNPHD, were used in this study from the USDA-ARS-National Animal Germplasm Program and Sul Ross University. Figure 2 presents the sources of Hereford data.

The 577 Hereford cattle described in the previous paragraph and 45,066 SNP common genotypes between BovineSNP50 and BovineSNPHD BeadChips formed the preliminary working data. These biallelic genotypes were converted to A/B format following the recommendations from Illumina, Inc.

(http://www.illumina.com/documents/products/technotes/technote_topbot.pdf) to guarantee uniformity in the reporting of allele frequency.

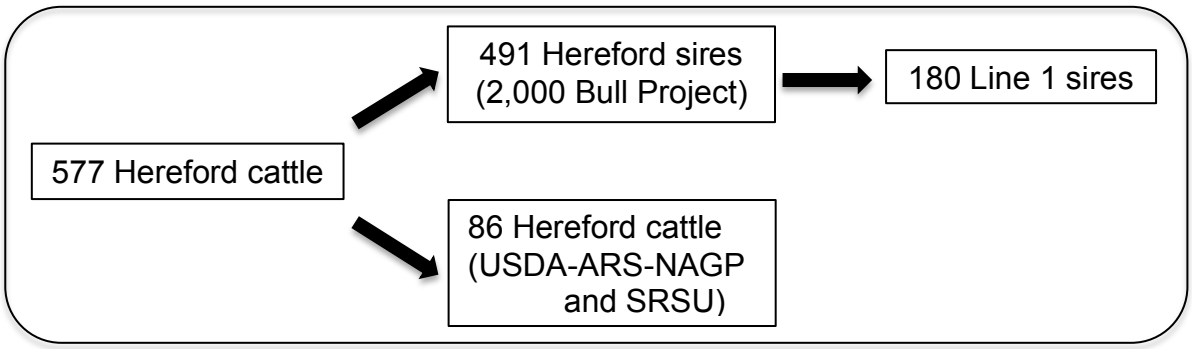

Figure 2. Sources of Hereford data used to perform a fine-scale genetic structure analysis.

Inspection of the pedigrees of the Hereford cattle (n = 577) indicated a substantial bias in the samples due to L1 Domino influence and use of that line across climate zones. In order to reduce this bias, a Bayesian analysis using STRUCTURE was performed (Pritchard et al., 2000; Hubisz et al., 2009). Cattle with a posterior probability of $\leq$ 0.37 in relation to the Line 1 pedigree were included in the analyses. The remaining 278 Hereford cattle were assigned to climate zones (climate zone explanation in subsequent sections). Hereford cattle were assigned to the climate zone using location of their respective breeder. Coefficients of genetic relationships within and among climate zones were calculated until each ancestor was unknown (Table 1). Hereford cattle with > 0.40 genetic relationship across climate zones were removed from the data leaving 225 animals. An alternative method using the similar cattle (i.e. Hereford cattle without high representation of Line 1 pedigree), climate zones, and genotype data was also investigated; see supplementary material.

Table 1. Coefficients of relationships of Hereford cattle without high representation of the Line 1 pedigree (n = 278).

Climate Zone	Cool Arid	Cool Humid	Transition Zone	Warm Arid	Warm Humid
Cool Arid	0.11				
Cool Humid	0.11	0.13			
Transition Zone	0.11	0.12	0.14		
Warm Arid	0.12	0.12	0.13	0.12	
Warm Humid	0.10	0.11	0.12	0.12	0.13

Table 2 presents the EPD and accuracy of eight growth and carcass traits of Hereford cattle (n = 167). The discrepancy between the population size and number of records obtained was due to 58 Hereford cattle used in the analyses that were not registered; therefore, their pedigree information was not available. The average EPD accuracy of the Hereford cattle for the eight traits was 0.53 ± 4.31. According to Greiner (2013), to achieve an accuracy of 0.56 for a moderately heritable trait, 53 progeny records must be obtained on each animal. In theory, these data potentially represented 11,925 progeny.

Table 2. Eight growth and carcass traits and their corresponding expected progeny differences (EPD) and accuracies of Hereford cattle in each climate zone (n = 167; Accessed from the AHA March 23, 2016).

Trait	Cool Arid EPD	Cool Humid EPD	Transition Zone EPD	Warm Arid EPD	Warm Humid EPD	Average Accuracy
Birth Weight	4.37	4.23	3.96	2.45	2.67	0.7353
Weaning Weight	43.07	49.53	47.48	24.57	43.95	0.6646
Yearling Weight	70.85	80.39	76.47	50.10	72.01	0.6595
Calving Ease Direct	-1.11	-0.06	-0.59	0.10	1.50	0.4593
Calving Ease Maternal	0.83	0.55	0.92	1.40	-0.16	0.4268
Marbling	-0.02	-0.04	0.04	0.16	0.07	0.4046
Rib-eye Area	0.23	0.34	0.28	-0.05	0.09	0.4783
Fat	-0.01	-0.02	0.00	-0.01	0.00	0.4396

Single-Nucleotide Polymorphisms

Two SNP panels were evaluated in the Hereford cattle: 14,312 neutral SNP and 66 SNP associated to traits potentially responsive to climate. The 14,312 SNP were derived from the 45,066 genotype data common to BovineSNP50 and BovineHDSNP BeadChips. Quality control filtering (i.e., eliminator) of 45,066 genotype data was performed as follows: sample call rate < 0.85; minor allele frequency (MAF) < 0.05; Hardy-Weinberg Equilibrium (HWE) significance < 0.001; and linkage disequilibrium pruning of SNP within a 50 SNP window that had an r^2 >0.5. The subsequent fine-genetic structure analysis was performed with 14,312 SNP as the filtering procedure eliminated 30,754 genotypes. Figure 3 describes the procedures to derive the 14,312 SNP.

A panel of 66 SNP was used to test Hardy-Weinberg Equilibrium (HWE) and detection of loci under selection (DLS). The 66 SNP were chosen for evaluation based on their association to traits with a logical likelihood of being responsive to climate change. First, 705 quantitative trait loci (QTL; a section of DNA that is associated with phenotypic variation) associated with traits potentially influenced by climate were queried from CattleQTLdb (Hu et al., 2013). Traits initially included in data were heat stress, body temperature, respiration rate, degree of coat color spotting, body weight, white coat color spotting on back, early embryonic survival, milk yield, net merit, sperm count, oocytes that cleaved, blastocyte stage, daughter pregnancy rate, sperm mobility, sperm motility, heifer conception rate, cow conception rate, and cow productive life. However, some of the SNP associated with these QTL were not located in the 45,066

SNP panel used to evaluate the Hereford cattle. Therefore, 66 SNP that were located on the 45,066 SNP panel were identified for evaluation in Hereford cattle.

The 66 SNP were previously derived from QTL studies involving Holstein (n = 55), Braunvieh (n = 1), Brown Swiss (n = 5), and Hereford cattle (n = 5). Mature cow body weight SNP were associated with Hereford, whereas all other SNP obtained were derived from Holstein, Braunvieh, and Brown Swiss cattle.

Of the 66 SNP, 29 SNP were intronic, whereas no SNP were exonic (Kitts and Sherry, 2002). The remaining 37 SNP were intergenic. These SNP were located on 21 of the 30 chromosomes of *Bos taurus* animals. Table 3 presents information describing each of the 66 SNP.

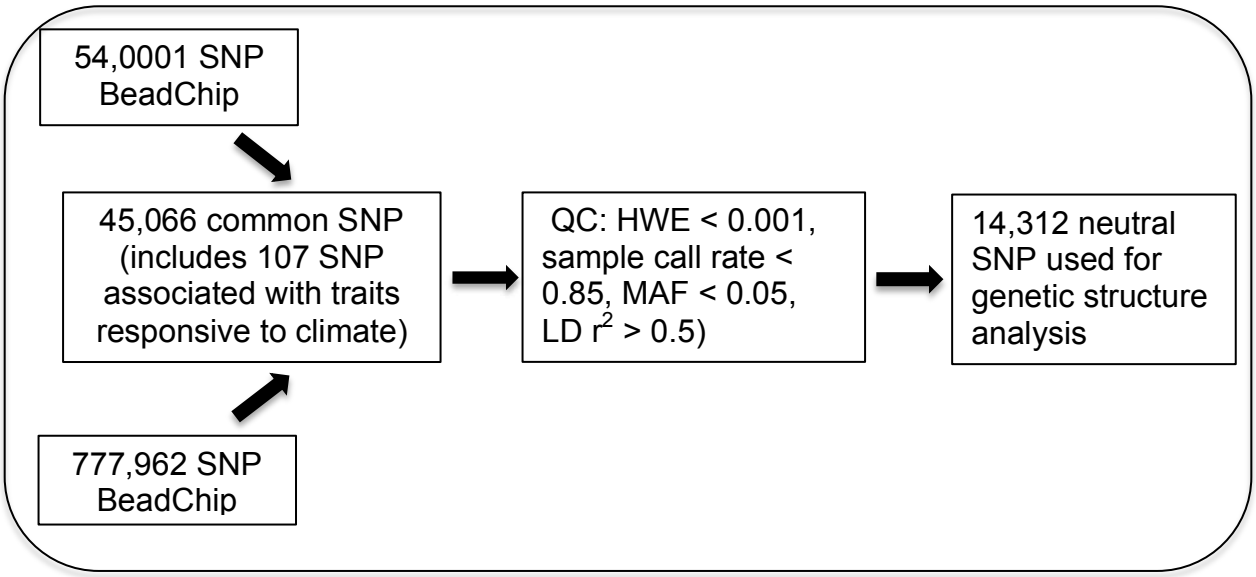

Figure 3. Diagram describing reduction of SNP from the BovineSNP50 BeadChip and BovineHD BeadChip to 14,312.

Table 3. Sixty-six SNP descriptions evaluated in Hereford cattle across five climate zones. These SNP were derived from the BovineSNP50 and BovineSNPHD BeadChips and were within QTL described in CattleQTLdb. (SNP Name = Name given to single-nucleotide polymorphism; SNP = reference SNP ID; BTA = *Bos taurus* autosomal; Locus = position of SNP on chromosome; Assembly = Source of SNP assembly).

SNP[1] Name	SNP	Trait	BTA[2]	Locus	Assembly	Breed	Source
ARS-BFGL-NGS-67327	rs110505759	Body Weight (mature)	3	72519744	UMD 3.1	Hereford	Saatchi et al., 2014
ARS-BFGL-NGS-41839	rs110564947	Body Weight (mature)	1	76416854	UMD 3.1	Hereford	Saatchi et al., 2014
ARS-BFGL-NGS-39379	rs110421124	Body Weight (mature)	5	106269362	UMD 3.1	Hereford	Saatchi et al., 2014
ARS-BFGL-NGS-18900	rs110059753	Body Weight (mature)	7	93218452	UMD 3.1	Hereford	Saatchi et al., 2014
ARS-BFGL-NGS-6079	rs110835938	Body Weight (mature)	7	21595908	UMD 3.1	Hereford	Saatchi et al., 2014
ARS-BFGL-NGS-97944	rs41711496	Daughter Pregnancy Rate	13	75567844	UMD 3.1	Holstein	Cochran et al., 2013
BTB-01271264	rs42397090	Early Embryonic Survival	8	27557552	UMD 3.1	Holstein	Huang et al., 2010
ARS-BFGL-NGS-45806	rs110721971	Early Embryonic Survival	12	37025686	UMD 3.1	Holstein	Huang et al., 2010
ARS-BFGL-NGS-103355	rs110464321	Early Embryonic Survival	13	19590132	UMD 3.1	Holstein	Huang et al., 2010
Hapmap58887-rs29013502	rs29013502	Heat Stress	24	28907154	UMD 3.1	Holstein	Dikmen et al., 2013
Hapmap47861-BTA-120563	rs41622115	Heat Stress	5	89472174	UMD 3.1	Holstein	Dikmen et al., 2013
Hapmap47403-BTA-76048	rs41567027	Heat Stress	6	45153190	UMD 3.1	Holstein	Dikmen et al., 2013
Hapmap46698-BTA-38760	rs41579673	Heat Stress	16	35317388	UMD 3.1	Holstein	Dikmen et al., 2013
Hapmap39941-BTA-70878	rs41573162	Heat Stress	4	64386271	UMD 3.1	Holstein	Dikmen et al., 2013

Hapmap30420-BTC-039335	rs109279094	Heat Stress	6	45175137	UMD 3.1	Holstein	Dikmen et al., 2013
BTB-01646599	rs42761380	Heat Stress	24	28941584	UMD 3.1	Holstein	Dikmen et al., 2013
BTB-01485274	rs42609685	Heat Stress	24	28877547	UMD 3.1	Holstein	Dikmen et al., 2013
BTB-01267080	rs42394542	Heat Stress	5	89512928	UMD 3.1	Holstein	Dikmen et al., 2013
BTB-01267042	rs42393904	Heat Stress	5	89568937	UMD 3.1	Holstein	Dikmen et al., 2013
BTB-00638221	rs41798380	Heat Stress	16	35272426	UMD 3.1	Holstein	Dikmen et al., 2013
BTA-27496-no-rs	rs41609304	Heat Stress	12	2500836	UMD 3.1	Holstein	Dikmen et al., 2013
ARS-BFGL-NGS-89847	rs110209659	Heat Stress	7	2457750	UMD 3.1	Holstein	Dikmen et al., 2013
ARS-BFGL-NGS-71584	rs42090237	Heat Stress	26	20290497	UMD 3.1	Holstein	Dikmen et al., 2013
ARS-BFGL-NGS-458	rs111023020	Heat Stress	4	64351574	UMD 3.1	Holstein	Dikmen et al., 2013
ARS-BFGL-NGS-41140	rs42042561	Heat Stress	24	28975828	UMD 3.1	Holstein	Dikmen et al., 2013
ARS-BFGL-NGS-35716	rs110012069	Heat Stress	24	29013292	UMD 3.1	Holstein	Dikmen et al., 2013
ARS-BFGL-NGS-29516	rs109002679	Heat Stress	23	14246801	UMD 3.1	Holstein	Dikmen et al., 2013
ARS-BFGL-NGS-23064	rs109890402	Heat Stress	26	20365711	UMD 3.1	Holstein	Dikmen et al., 2013
ARS-BFGL-NGS-16848	rs110076378	Heat Stress	28	2924302	UMD 3.1	Holstein	Dikmen et al., 2013
ARS-BFGL-NGS-108847	rs43719996	Heat Stress	16	58500249	UMD 3.1	Holstein	Dikmen et al., 2013
ARS-BFGL-NGS-107395	rs110333567	Heat Stress	29	47527067	UMD 3.1	Holstein	Dikmen et al., 2013
ARS-BFGL-NGS-106628	rs110691682	Heat Stress	16	35172005	UMD 3.1	Holstein	Dikmen et al., 2013
ARS-BFGL-NGS-10307	rs109477915	Heat Stress	26	20259486	UMD 3.1	Holstein	Dikmen et al., 2013
ARS-BFGL-NGS-100932	rs41798395	Heat Stress	16	35230105	UMD 3.1	Holstein	Dikmen et al., 2013

ARS-BFGL-NGS-100006	rs41568955	Heat Stress	23	14215024	UMD 3.1	Holstein	Dikmen et al., 2013
ARS-BFGL-NGS-34049	rs109262355	Heifer Conception Rate	20	35249040	UMD 3.1	Holstein	Cochran et al., 2013
UA-IFASA-6878	rs41629750	Milk Yield	14	1044040	BTAU 4.0	Holstein	Meredith et al., 2012
UA-IFASA-6228	rs110718625	Milk Yield	14	5204595	BTAU 4.0	Holstein	Meredith et al., 2012
Hapmap32236-BTC-049785	rs42215845	Milk Yield	14	5139497	BTAU 4.0	Holstein	Meredith et al., 2012
Hapmap32234-BTC-048199	rs108995214	Milk Yield	14	5640337	BTAU 4.0	Holstein	Meredith et al., 2012
Hapmap30646-BTC-002054	rs110060785	Milk Yield	14	1461084	BTAU 4.0	Holstein	Meredith et al., 2012
Hapmap30374-BTC-002159	rs109529219	Milk Yield	14	1546590	BTAU 4.0	Holstein	Meredith et al., 2012
Hapmap30086-BTC-002066	rs110199901	Milk Yield	14	1490177	BTAU 4.0	Holstein	Meredith et al., 2012
Hapmap29888-BTC-003509	rs110237430	Milk Yield	14	1154381	BTAU 4.0	Holstein	Meredith et al., 2012
Hapmap26598-BTC-062212	rs41597129	Milk Yield	14	6567156	BTAU 4.0	Holstein	Meredith et al., 2012
Hapmap24715-BTC-001973	rs110323635	Milk Yield	14	856890	BTAU 4.0	Holstein	Meredith et al., 2012
Hapmap23454-BTC-046932	rs108971409	Milk Yield	14	4182817	BTAU 4.0	Holstein	Meredith et al., 2012
BTA-35941-no-rs	rs41627764	Milk Yield	14	894253	BTAU 4.0	Holstein	Meredith et al., 2012
ARS-BFGL-NGS-94706	rs17870736	Milk Yield	14	281534	BTAU 4.0	Holstein	Meredith et al., 2012
ARS-BFGL-NGS-4939	rs109421300	Milk Yield	14	443936	BTAU 4.0	Holstein	Meredith et al., 2012
ARS-BFGL-NGS-3571	rs110351374	Milk Yield	14	3587017	BTAU 4.0	Holstein	Meredith et al., 2012

ARS-BFGL-NGS-34135	rs109968515	Milk Yield	14	260342	BTAU 4.0	Holstein	Meredith et al., 2012
ARS-BFGL-NGS-26520	rs109617015	Milk Yield	14	996983	BTAU 4.0	Holstein	Meredith et al., 2012
ARS-BFGL-NGS-107379	rs109350371	Milk Yield	14	679601	BTAU 4.0	Holstein	Meredith et al., 2012
ARS-BFGL-NGS-102953	rs110856800	Milk Yield	14	5867265	BTAU 4.0	Holstein	Meredith et al., 2012
ARS-BFGL-NGS-100480	rs110017379	Milk Yield	14	2607582	BTAU 4.0	Holstein	Meredith et al., 2012
ARS-BFGL-BAC-24804	rs110236070	Milk Yield	14	4157676	BTAU 4.0	Holstein	Meredith et al., 2012
Hapmap32136-BTA-160383	rs110220642	Milk Yield	4	92705191	UMD 3.1	Braunvieh	Maxa et al., 2012
Hapmap48796-BTA-51083	rs41635833	Milk Yield	20	63120443	UMD 3.1	Brown Swiss	Guo et al., 2012
Hapmap47184-BTA-114107	rs41613557	Milk Yield	5	33173961	UMD 3.1	Brown Swiss	Guo et al., 2012
Hapmap33541-BTC-016426	rs111008794	Milk Yield	25	1431881	UMD 3.1	Brown Swiss	Guo et al., 2012
ARS-BFGL-NGS-56044	rs110529685	Milk Yield	24	43170091	UMD 3.1	Brown Swiss	Guo et al., 2012
ARS-BFGL-NGS-3562	rs109557202	Milk Yield	25	1489008	UMD 3.1	Brown Swiss	Guo et al., 2012
Hapmap38412-BTA-50496	rs41581070	Milk Yield	20	37468100	UMD 3.1	Holstein	Chamberlain et al., 2012
BTA-50482-no-rs	rs41581068	Milk Yield	20	36336225	UMD 3.1	Holstein	Chamberlain et al., 2012
BTA-37177-no-rs	rs41583256	Milk Yield	15	58775396	UMD 3.1	Holstein	Chamberlain et al., 2012

[1] SNP: Single-Nucleotide Polymorphism.
[2] BTA: *Bos taurus* autosomal. The SNP and the locus were derived from CattleQTLdb: http://www.animalgenome.org/cgi-bin/QTLdb/BT/index (Hu et al., 2013).

Climate Zones

The conterminous U.S. has been separated into climate zones due to various climatic and plant topographies (Omernik and Griffith, 2014). The U.S. can be accurately divided into zones ranging from a few to 30 biomes (Peel et al., 2007). Hereford cattle (n = 278) were allocated to five climate zones which included Cool Arid (CA), Cool Humid (CH), Transition Zone (TZ), Warm Arid (WA), and Warm Humid (WH).

The CA zone is located in the northwestern region of the U.S. and reaches approximately 15 states engulfing the majority of the Rocky Mountains. The CH zone includes approximately 20 states located in the northwest and northeast regions of the U.S. This zone does not span all the northern states of the U.S., but borders both Pacific and Atlantic Ocean coastlines. Due to its location near the coasts, the CH region tends to have a more humid climate relative to the states not bordering the coastlines. The WA zone is located in the southwestern region of the U.S. and encompasses six states. These states are located in a desert region spanning from western Texas to California. The WH zone contains the southeastern part of the U.S. including states of Louisiana, Arkansas, eastern Texas, Alabama, Georgia, Florida, and South Carolina. This region tends to have a subtropical climate. Lastly, the TZ is located south of the CH zone and north of the WH zone, representing the east central region of the US. The TZ fits a unique area between warm, cool, arid, and humid climates. The contiguous U.S. and its corresponding regions are shown in Fig. 4.

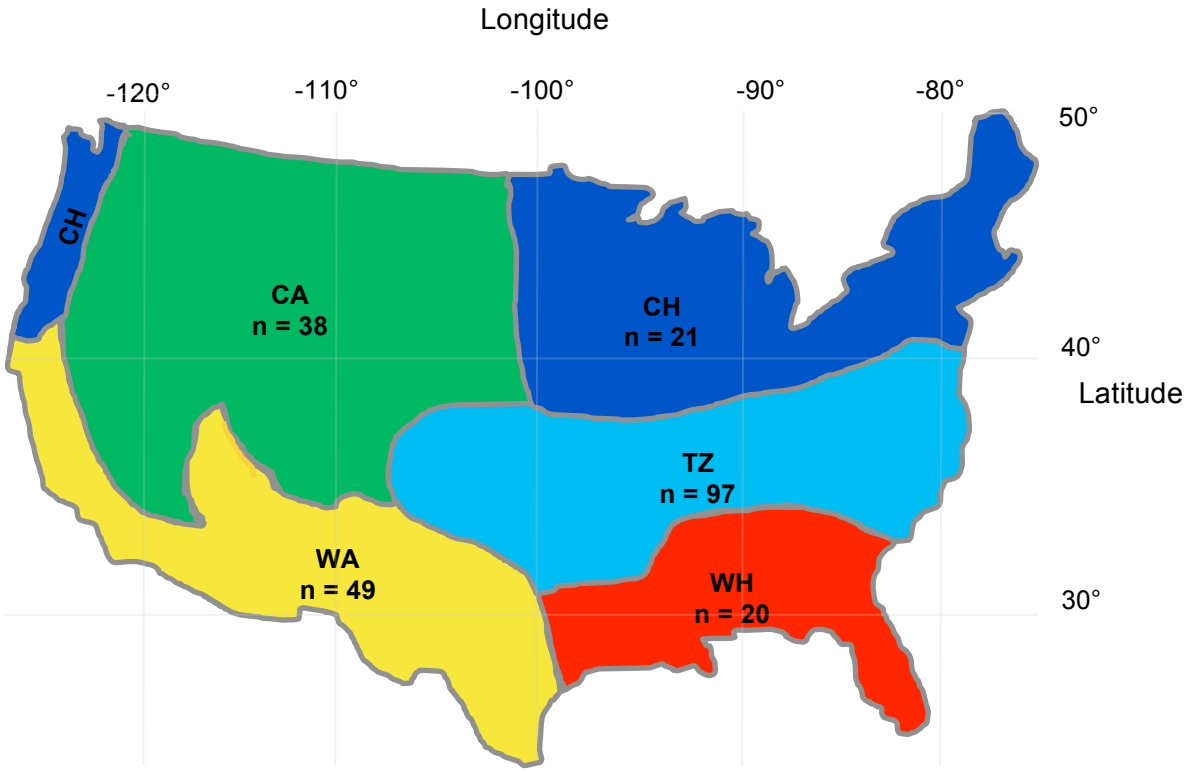

Figure 4. Five U.S. climates zones based broadly upon Köppen-Geiger climate classifications (Peel et al., 2007; CA = Cool Arid; CH = Cool Humid; TZ = Transition Zone; WA = Warm Arid; and WH = Warm Humid)

Climate information for the U.S. was obtained from the National Oceanic and Administrative Association to determine the thermal stress Hereford cattle in differing climate regions may have endured (Arguez et al., 2012; Menne et al., 2012). The temperature-humidity index (THI) has been formulated to represent the combined effects of thermal stress and was calculated as follows (Bohmanova et al., 2007):

$$THI=(1.8xT+32)-((0.55-0.0055xRH) \times (1.8xT-26))$$

Monthly measurements of afternoon average relative humidity (RH, %) ranging from 1938 to 2014 and normal daily maximum temperature (T, °C) ranging from 1981 to 2010 were acquired for every state within each of the five climate zones. First, weather information was gathered from 90 cities that contained weather information located nearest to the Hereford breeder location. Next, climate variables from states and regions that did not contain Hereford breeders were obtained from the most central weather station in that region. Highest temperatures typically occur in the afternoon, therefore, afternoon RH was used to calculate THI to achieve peak stress level. Lastly, temperature and humidity values were used to formulate the THI for every month of the year. Thermal stress was represented as four THI heat stress categories: Normal <75; Alert: 75-78; Danger: 79-83; and Emergency: >84 (LCI, 1970). Figure 5 represents the average THI measurements of each climate zone from January to December.

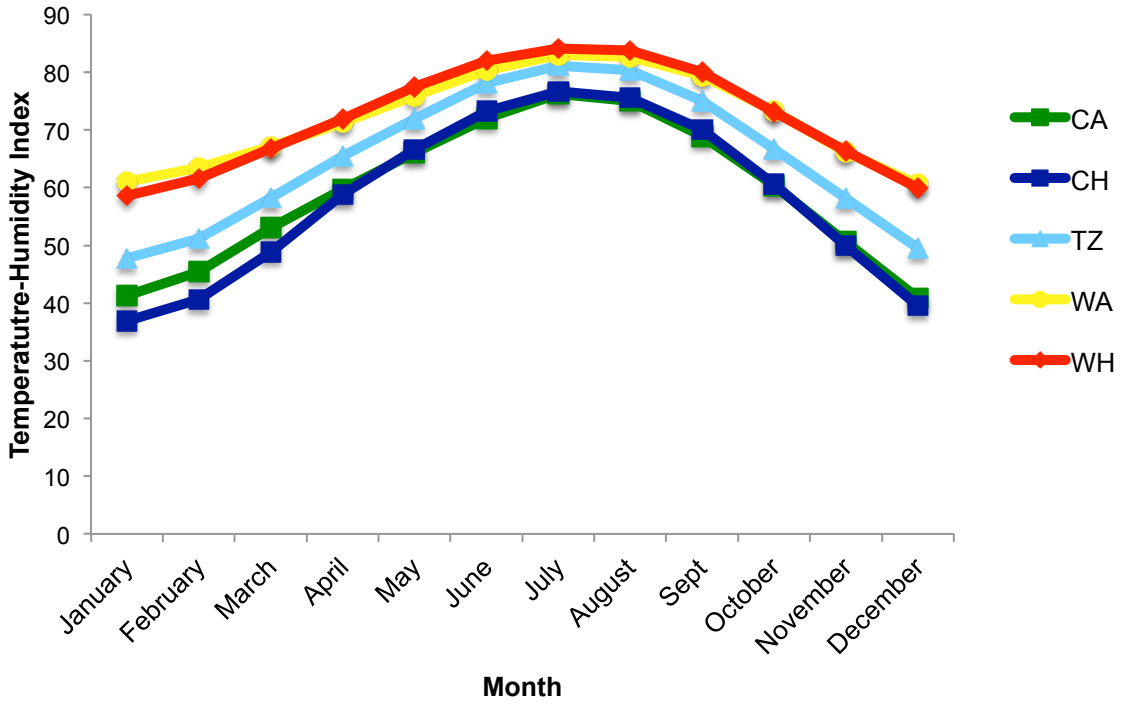

Figure 5. Average annual temperature-humidity index from January to December for five U.S. climate zones in which Hereford cattle reside (n = 225). The WA and WH zones are in the THI danger stress zone for five months out of the year. (CA = Cool Arid; CH = Cool Humid; TZ = Transition Zone; WA = Warm Arid; and WH = Warm Humid)

Analyses

Genetic structure of Hereford cattle was evaluated with ADMIXTURE 1.3 and the 14,312 SNP previously obtained. It was used as a cross-validation for values of *K* from 1 through 11 with 10 repetitions for each value of *K*. ADMIXTURE 1.3 is used to estimate population ancestry using SNP genotype data of unrelated individuals (Alexander et al., 2009). By utilizing this methodology, genetic structure within the population can be identified. The lowest cross-validation error of all the *K* values represents the most appropriate number of subpopulations within the data.

A population genetics analysis was performed using 66 SNP. Allele frequencies of the 66 SNP panel were calculated using GENALEX software and tested for HWE and detection of loci (DLS) under selection using ARLEQUIN (Peakall and Smouse, 2012; Excoffier and Lischer, 2010). By testing for HWE, SNP allele frequencies that have potentially been influenced by evolutionary processes can be identified and analyzed. The HWE locus-by-locus test was performed using 1,000,000 Markov chain steps and 10,000 dememorization steps. The DLS analysis was performed with 100 simulated demes and 50,000 coalescent simulations. The DLS analysis was used to detect genetic diversity and differentiation within and between populations (Excoffier et al., 2009). The SNP considered significant ($P < 0.05$) for the HWE and DLS analysis were further evaluated in ARLEQUIN for genetic differentiation through an analysis of molecular variance (AMOVA) with 10,000 permutations for significance and 1,000 permutations for the Mantel test (Excoffier and Lischer, 2010). The AMOVA test analyzed the significant SNP for the amount of population genetic substructure. In addition, a population pairwise matrix based on Wright's Fixation Index (F_{ST}) was constructed with the significant HWE and DLS SNP to estimate the genetic distances between populations. Figure 6 represents the Hereford analyses and the softwares that were used to perform analyses. Table 4 represents the models and assumptions used for genetic structure analyses of Hereford cattle.

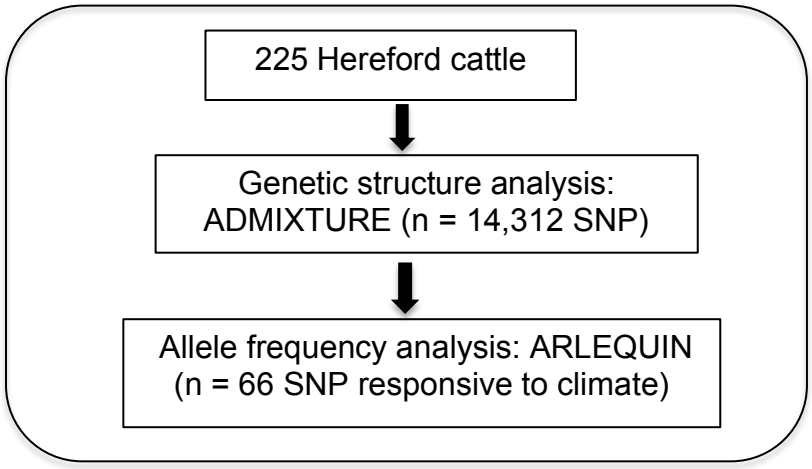

Figure 6. Description of SNP-based analyses used to evaluate Hereford cattle (n = 225).

Table 4. Description of the models and assumptions used for genetic structure analyses of Hereford cattle (n = 225).

Software	Function	Assumptions
Arlequin	Intra-population tests: Hardy-Weinberg Equilibrium: test of non-random association of alleles within diploid individuals. Inter-population tests: AMOVA: different hierarchical Analyses of Molecular Variance to evaluate the amount of population genetic structure; Detection of loci under selection: Detection of loci under selection by the examination of the joint distribution of F_{ST} and heterozygosity under a hierarchical island model; F_{ST}-Pairwise genetic distances: F_{ST} based genetic distances for short divergence time.	Hardy-Weinberg Equilibrium: population is large; no gene flow between populations, mutations are negligible, individuals are mating randomly, no natural selection. AMOVA: does not require normality. Detection of loci under selection: assumes no hierarchical structure. (Excoffier et al., 1992) F_{ST}-Pairwise genetic distances: random sampling to create the initial subdivisions at each level, no migration (Excoffier et al., 1992)
Genalex	Calculated allele frequencies and heterozygosity of codominant loci	
Admixture	This software uses maximum likelihood estimate of individual ancestries from multilocus SNP genotype datasets.	Assumes linkage equilibrium among markers.

Results

Fine-genetic structure analysis was performed using ADMIXTURE (Alexander et al., 2009) and 14,312 SNP and revealed that there were six clusters within the Hereford cattle (Fig. 7). The results reflected an association between population clusters and climate zones. Cluster 1 had large proportional assignments from both CA and CH climate zones (~40%). Cluster 2 was more prevalent in the arid zones with a 50% assignment in WA and 17% assignment for CA. All climate zones had representation in clusters 3, 4 and 5. The TZ tended to have the highest and WA the lowest proportional assignment among the three clusters. Cluster 6 had higher representation in the WH and WA climate zones, but was present across all climate zones but in varying proportions.

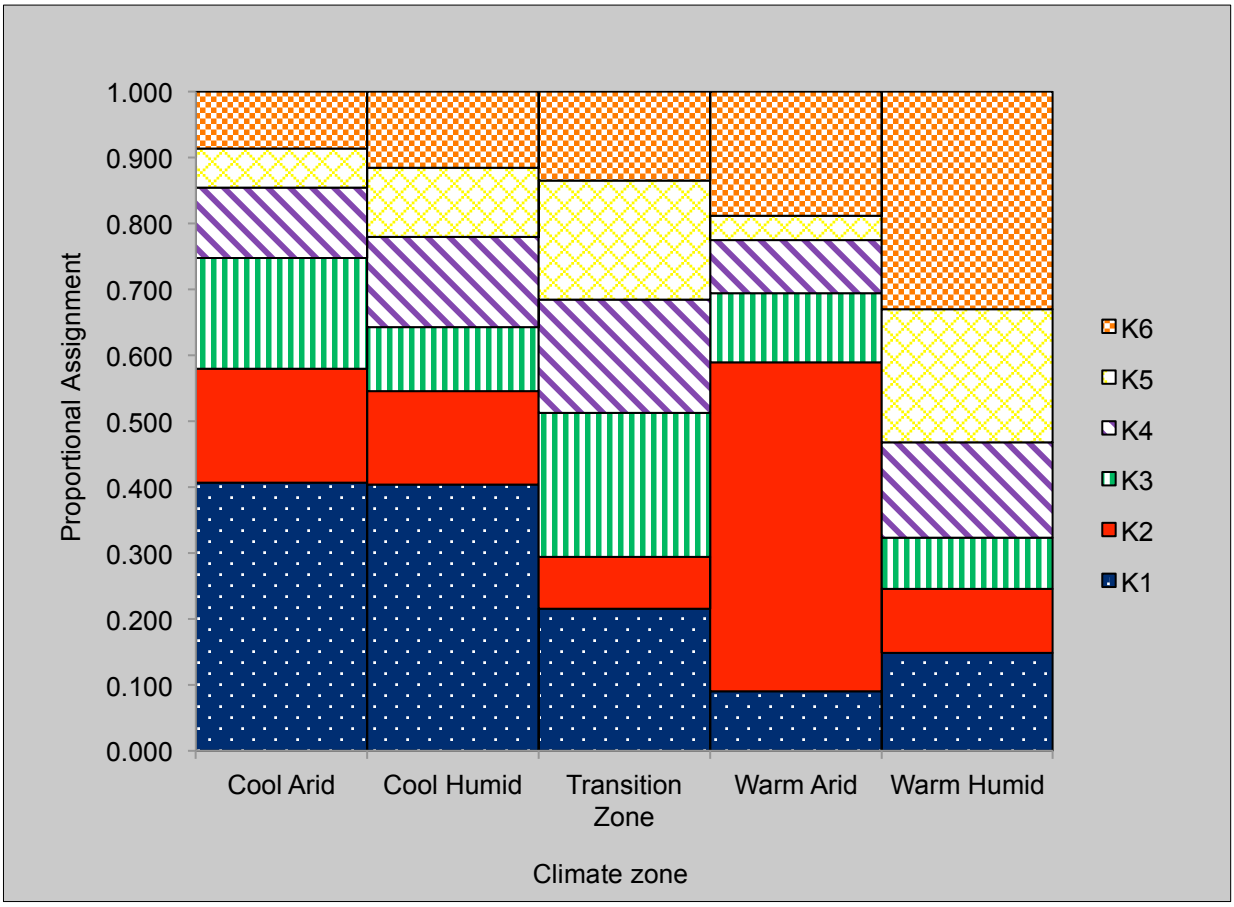

Figure 7. ADMIXTURE assignment of 6 clusters of 225 Hereford cattle based upon 14,312 SNP. The K value represents the proportion of the population detected.

Hereford cattle heterozygosity values for the 66 SNP potentially influenced by climate are presented in Table 5. The average observed heterozygosity for the 14,312 SNP panel was 0.359 ± 0.0010.

Table 5. Assignment and population heterozygosity for Hereford cattle allocated to five U.S. climate zones based on breeder location.

Climate Zone	Number of cattle	Heterozygosity
Cool Arid	38	0.364
Cool Humid	21	0.339
Transition Zone	97	0.338
Warm Arid	49	0.352
Warm Humid	20	0.337

Analyses of the 66 SNP associated with traits potentially influenced by climate in Hereford cattle revealed that 15 SNP were not in HWE and (or) under selection pressure (DLS). Population pairwise F_{ST} (i.e. Wright's Fixation Index; estimates genetic distance) were calculated for climate zones using the 15 significant loci (Table 6). The F_{ST} values between CA and CH and TZ were not statistically significant. Additionally, the F_{ST} value was not statistically significant for CH and TZ and WH climates zones. There was low differentiation between CA and WA, CA and WH, and TZ and WA climate zones as indicated by the significant F_{ST} values. However, there was moderate differentiation between CH and WA, and WA and WH climate zones (Holsinger and Weir, 2009). Interestingly, the coefficients of relationships represented in Table 1 revealed a higher relationship between TZ and WA (i.e., 0.13), and lowest coefficient of relationship between climate zones CA and WH (i.e., 0.10).

Table 6. Average population differentiation (F_{st}) due to genetic substructure (15 SNP) in Hereford cattle (n = 225) across U.S. climate zones.

	Region				
Region	Cool Arid	Cool Humid	Transition Zone	Warm Arid	Warm Humid
Cool Arid	0.00000				
Cool Humid	0.00540	0.00000			
Transition Zone	0.00097	-0.00825	0.00000		
Warm Arid	0.02550*	0.05667*	0.04306*	0.00000	
Warm Humid	0.01585*	0.00013	0.00710	0.09793*	0.00000

*$P < 0.05$

Table 7 represents the 15 SNP evaluated in AMOVA comparisons. Allelic frequencies for SNP that were significant via AMOVA comparisons (P < 0.05) were evaluated among climate zones (n = 7; Fig. 8). Warm Arid and WH subpopulations appeared to be at opposite extremes especially for SNP associated with heat stress. The allele frequencies for the heat stress SNP appeared to be intermediate for the TZ, CA, and CH zones. Allele frequencies of SNP associated with milk yield, body weight, and heifer conception rate showed no distinct pattern, but differed among climate zones. There is evidence of genetic structure of Hereford cattle assigned to climate zone, especially for SNP associated with heat stress.

Table 7. Analysis of molecular variance of 15 SNP significant for Hardy-Weinberg Equilibrium and detection of loci under selection in 225 Hereford cattle assigned to five U.S. climate zones. (MY = Milk Yield; BW = Body Weight; HS = Heat Stress; HCR = Heifer Conception Rate)

SNP[1]	F_{st} value	P-value
MY: rs110220642	0.0528	< 0.0001*
HS: rs42394542	-0.0067	0.8200
BW: rs110421124	0.0269	0.0197*
HS: rs109279094	-0.0034	0.5994
MY: rs109968515	-0.0069	1.0000
MY: rs42215845	-0.0102	0.9556
HCR: rs109262355	0.0347	0.0093*
MY: rs41635833	-0.0040	0.6253
HS: rs42609685	0.0751	< 0.0001*
HS: rs42761380	0.0513	0.0006*
HS: rs110012069	0.0191	0.0474*
MY: rs109557202	0.0029	0.3491
HS: rs110333567	0.0565	0.0003*

*Loci significant for AMOVA analysis: $P < 0.05$

[1]Loci with one allele include HS: ARS-BFGL-NGS-89848 and MY: ARS-BFGL-NGS-4939 and were not tested.

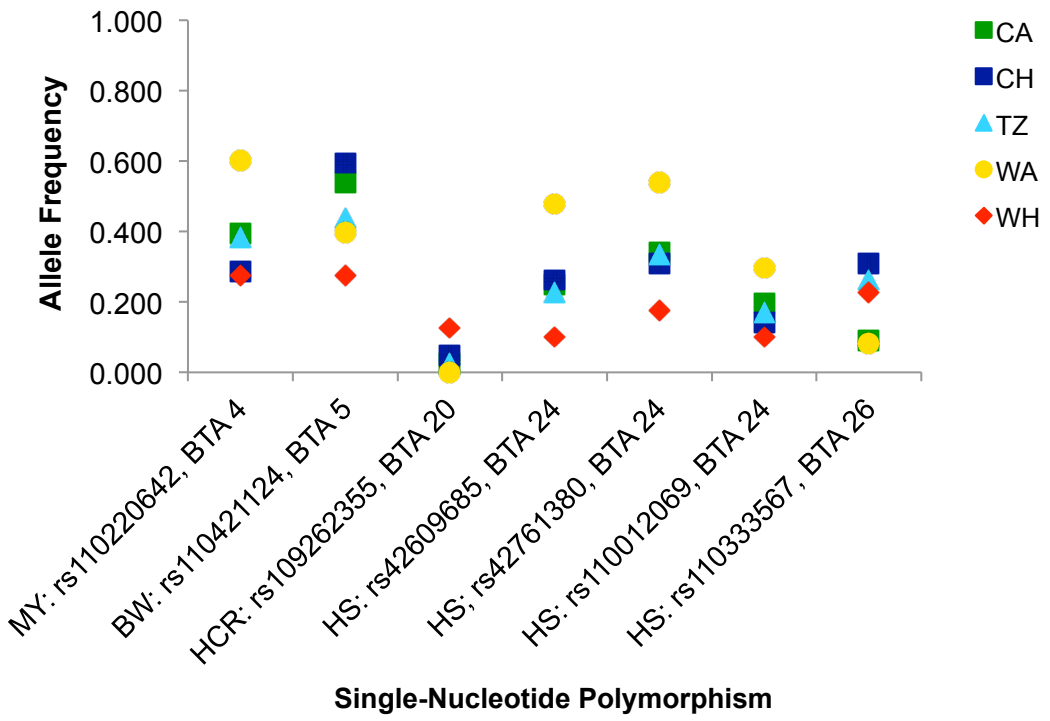

Figure 8. Frequencies of the "A" allele (genotypes in A/B format) among five U.S. climate zones from loci that were significant in AMOVA comparisons (n = 7). The x-axis represents trait, single-nucleotide polymorphism reference ID, and chromosome number. (BTA = *Bos taurus* autosomal; MY = Milk Yield; BW = Body Weight; HS = Heat Stress; CA = Cool Arid; CH = Cool Humid; TZ = Transition Zone; WA = Warm Arid; and WH = Warm Humid).

Discussion

This study tested a hypothesis that Hereford cattle assigned to five U.S. climate zones contain a SNP-based genetic substructure influenced by climate. The SNP allele frequencies were analyzed to determine the genetic diversity among the cattle assigned to each climate zone. Although SNP allele frequencies can be used to determine the effect of loci on a trait (on an individual SNP or aggregate level), the SNP allele frequencies in the present study were used to determine if there were significant differences of allele frequencies between climate zone that may be indicative of regional adaptation. Results of the current study showed genetic diversity in the population

based on the allele frequencies of the SNP (Table 6, Fig. 8). For example, Table 6 represented differentiation between climate zones based on the 15 SNP allele frequencies analyzed using F_{ST} measures. Additionally, Fig. 8 revealed the allele frequency differences between climate zones. Varying allele frequencies among the subpopulations could potentially increase selection pressure for the most favorable genotypes. For example, bulls that are proven for specific traits in one environment may become more relevant in that respective climate zone. In contrast, bulls that are not proven for specific traits in a climate zone, may become less desirable in that environment.

Table 6 revealed low to moderate differentiation between climate zones for the 15 SNP observed. The relationships between TZ and other climate zones were insignificant, with the exception of the WA climate zone. Interestingly, Table 6 revealed moderate differentiation between arid and humid zones (i.e., CH and WA; WA and WH). However, CH and WA, and WA and WH coefficients of relationships were 0.12, the second highest relationship between climate zones observed in the Hereford population. Although these climate zone relationships were the highest, it appears that other forces may be influencing the allele frequency differences between the humid and arid climate zones. For example, the allele frequency differences between the WA and WH climate zones suggested that the cattle in these two zones are producing under differing environments, although their THI was similar (Fig. 5). Because of its geographical relationship to the arid and humid zones, the TZ may be able to provide robust genotypes that are less sensitive to the varying environmental conditions, hence their intermediate allele frequencies reported in Fig. 8. The SNP found to violate HWE

and DLS in addition to the F_{ST} differences between climate zones showed evidence of regional allelic differences.

Although genetic substructure was observed across climate zones, the utilization of the Hereford breed and the 66 SNP panel may have influenced the results of the current study. Hereford cattle have existed for 199 years within the U.S. (AHA, 2016), whereas other breeds, such as Charolais, were introduced into the U.S. only 82 years ago (AICA, 2016) and have fewer generations of selection. The time-frame of the Hereford breed in the U.S. and the selection that has occurred could be responsible for the genetic structure observed.

Cleveland et al. (2005) reported that inbreeding levels in Hereford cattle increased rapidly from 1900 to 1945 with a maximum of 11.5% inbreeding in 1966. This increase in inbreeding and selection for smaller cattle in the 1940s led to the increased observation of genetic abnormalities such as Snorter dwarfism. This recessive autosomal trait inhibits normal vertebral or nasal development, resulting in a small, deformed calf that “snorts” when breathing (Marlowe 1964; Whitlock et al., 2008). Producers were unknowingly selecting for the heterozygous cattle at the Snorter dwarfism locus, which ultimately led to the increased expression of the abnormality across the breed (Marlowe, 1964).

While historical and recent reports have shown that Hereford cattle have endured intense selection and relatively high inbreeding levels (Purfield et al., 2012; Cleveland et al., 2005), the present study’s results revealed regional genetic diversity, which may be indicative of plastic genotypes that allow Hereford cattle to acclimate to varied environments.

The observed heterozygosity levels of SNP within the Hereford cattle appeared similar to other *Bos taurus* breeds (0.310 to .362). The observed heterozygosity levels of microsatellites within breeds of sheep (0.22 – 0.38; Lin et al., 2010; Kijas et al., 2012) also appeared similar to heterozygosity levels within the Hereford population. However, heterozygosity levels for bovine were similar to less than the calculated heterozygosity levels of microsatellites found in purebred swine (0.35 to 0.74; Laval et al., 2000; Thuy et al., 2006; Nidup and Moran, 2011). There is evidence that breeders have implemented selection strategies to improve growth traits, such as weaning weight and yearling weight, and breeding values have increased since the induction of EPDs (AHA, 2016, RAAA, 2016). However, EPD measurements have not, in general, been utilized to combat climate changes (RAAA, 2016; AHA; 2016). Although the 66 SNP utilized to calculate heterozygosity were associated with traits possibly influenced by climate, Hereford cattle heterozygosity for the 66 SNP panel was similar to the average heterozygosity calculated for the neutral 14,312 SNP panel (i.e., 0.359 ± 0.001).

The SNP used in this study were mostly related to body weight, heat stress, and milk yield traits. Though genetic structure was observed in these traits, it may be more informative to use traits such as slick hair, respiratory rate, hair pigmentation, body temperature, or white coat color spotting to study the impact of climate on animal genotypes. However, some of the QTL obtained that pertained to these traits had no peak SNP or were not included in the 45,066 SNP panel. Since the advent of genomic selection and GWAS, QTL pertaining to climate have been limited mostly to physical traits influenced by climate. As accrual molecular genetic studies continue, QTL directly responsive to climate will be more informational when performing G x E studies.

Additionally, the 66 SNP were previously derived from Holstein, Braunvieh, Brown Swiss, and Hereford cattle. Of the traits evaluated, most of the trait and SNP associations were derived from dairy cattle. These cows are generally kept in concentrated animal feeding operations where high quality feed, shelter, and sometimes shade and misters are available to alleviate heat stress. In comparison to the present study, Hereford cattle resided mostly in pastures or extensive rangeland where grazing was their main source of food and shelter was mostly dependent on topography. It would be beneficial to obtain SNP that were discovered in rangeland cattle to determine if other SNP and trait associations pertaining to climate are discovered.

Hereford cattle are widely used throughout the world (AHA, 2016; DAD-IS, 2016). According to the American Hereford Association (2014), 80% of the cows in Uruguay are Hereford. The widespread use of the Hereford breed led to the initial Pan-American genetic evaluation for Hereford cattle in 2014. This genetic evaluation contained Hereford cattle from the U.S., Canada, Uruguay, and Argentina. Therefore, evaluation of predominant AI Herefords sires within the present analysis may potentially become more informational for global marketing opportunities for Hereford germplasm in differing environments. For example, Hereford cattle that are thriving in specific environments within the U.S. may be useful in other countries with similar climates.

Efforts to decrease gene flow were made in the present study (i.e., eliminate cattle with high representation of Line 1 pedigree). Additionally, the studied 66 SNP potentially influenced by climate were used to evaluate climate impacts on the cattle. By filtering the SNP and the cattle evaluated, some of the genetic connectivity was eliminated within the breed. Shane Bedwell (personal communication, AHA, 2016) from

the American Hereford Association reported that 31.1% of the 2015 Hereford cattle calf crop was a result of AI. In comparison to the American Angus Association (i.e., the largest breed registry within the U.S.), 53% of their 2015 calf crop was the result of AI. The modest AI rate within Hereford cattle may suggest regional natural service breeding strategies across the U.S. forming the observed genetic substructure. As suggested by Mulder et al. (2006), specialized genotypes for each environment may be required to continue production as climate impacts progress, thus increasing the utilization of proven genotypes within a specific climate.

Conclusions

Fine-scale genetic substructure based on five U.S. climate zones was found within the Hereford cattle using two SNP panels. The genetic diversity observed within the subpopulations for each climate zone provides beef cattle producers with more opportunities to select for animals that will be more productive in their unique climate zones. Specifically, cattle in the TZ may contain the plasticity needed to serve a multitude of environments and improve production in warmer climate zones. Based on genetic structure and allele frequency results, we accept our hypothesis that Hereford cattle residing in five U.S. climate zones contain a SNP-based genetic substructure influenced by climate.

CHAPTER 4: EVALUATION OF GENETIC STRUCTURE ACROSS FIVE U.S. CLIMATE ZONES USING PROMINENT AI SIRES OF RED ANGUS CATTLE

Introduction

Global climatic change makes understanding gene by environment interactions (G x E) important for sustaining livestock production. Cattle performance in diverse climates can be problematic if cattle do not possess genotypes that confer environmental adaptability. Genetic diversity aids livestock populations in responding to their environment and is vital to their survival (Robinson e al., 2009; Gaughan et al., 1999).

By conducting an in-depth genotypic analysis, the genetic structure of cattle populations in relation to climate can be assessed. This includes analyzing allele frequencies of SNP that are potentially influenced by climate. Preceding research revealed that Hereford cattle appeared to have genetic substructure that corresponded to five major climate zones of the U.S. (Chapter 3; Krehbiel et al., 2015; Krehbiel et al., 2016). This genetic substructure was determined with a 14,312 neutral SNP panel and allele frequencies of 66 SNP associated with traits that could be influenced by climate zone (i.e., milk yield, mature cow body weight, heat stress, early embryonic survival, etc.). Observing this substructure suggested that there were allele frequencies of the SNP unique to each of the climates zones. To characterize the diversity in another British *Bos taurus* breed, population genetic parameters were estimated in Red Angus cattle.

The hypothesis of this research was that prominent Red Angus AI sires would possess genetic substructure across the five U.S. climate zones as evaluated in

Chapter 3. To test the hypothesis, a fine-scale genetic structure analysis was performed in the Red Angus sires. Another objective was to compare alleles of Red Angus sires to Hereford cattle in Chapter 3.

Materials and Methods

Cattle evaluated and genotyping

Cattle studied in this project were from the 2,000 Bull Project (n = 175; Kuehn, et al., 2011), which involved influential AI sires within the U.S. Beef Industry. The corresponding breed associations chose the sires included in the 2,000 Bull Project based upon their predominance within the industry. Therefore, sires evaluated in the present study were not evenly sampled. The 175 sires were derived from 71 breeders representing 18 states in the U.S. These data contained sires of birth years 1978 to 2007, representing approximately 6 generations. Sires were genotyped using the BovineSNP50 BeadChip (54,001 SNP; Matukumalli et al., 2009). Coefficients of genetic relationships within and among climate zones were calculated until each ancestor was unknown (Table 8).

Table 8. Coefficients of relationships for Red Angus sires (n = 174).

Climate Zone	Cool Arid	Cool Humid	Transition Zone	Warm Arid
Cool Arid	0.08			
Cool Humid	0.08	0.11		
Transition Zone	0.10	0.10	0.12	
Warm Arid	0.07	0.08	0.08	0.14

Single-Nucleotide Polymorphisms

Two SNP panels were evaluated in Red Angus cattle: 13,960 neutral SNP and 66 SNP associated with traits responsive to climate. The 13,960 SNP were used to

determine population structure, whereas the 66 SNP were used to test Hardy-Weinberg Equilibrium (HWE) and detect loci under selection (DLS).

The 13,960 SNP were derived from genotypes of the BovineSNP50 BeadChip. Quality control filtering (i.e., eliminator) was applied to the genotype data and eliminated SNP based on the following analyses: minor allele frequency (MAF) < 0.05; sample call rate < 0.95; Hardy-Weinberg Equilibrium (HWE) < 0.001; and linkage disequilibrium pruning SNP within a 50 SNP window that had r^2 >0.4. The subsequent fine-scale genetic structure analysis using ADMIXTURE was performed with 13,960 SNP as the filtering procedure eliminated 40,040 genotypes (Pritchard et al., 2000; Hubisz et al., 2009).

The 66 SNP previously used in study of Hereford cattle were also evaluated in Red Angus sires. These 66 SNP were selected from previous reports suggesting their association with traits potentially influenced by climate. Single-nucleotide polymorphism selection and information was outlined in Chapter 3. Traits evaluated included: mature cow body weight, heat stress, heifer conception rate, milk yield, and embryonic survival.

Climate Zones

Red Angus bulls (n = 175) were assigned to one of the five climate zones in the U.S. based upon breeder location and coded as following: Cool Arid (CA), Cool Humid (CH), Transition Zone (TZ), Warm Arid (WA), and Warm Humid (WH). Full description of the climate zones was outlined in Chapter 3. Sires were not evenly distributed across the five U.S. climate zones (Fig. 9). Due to the small distribution of sires to the WH region, this animal and region was omitted from the data, leaving 174 sires and four climate regions.

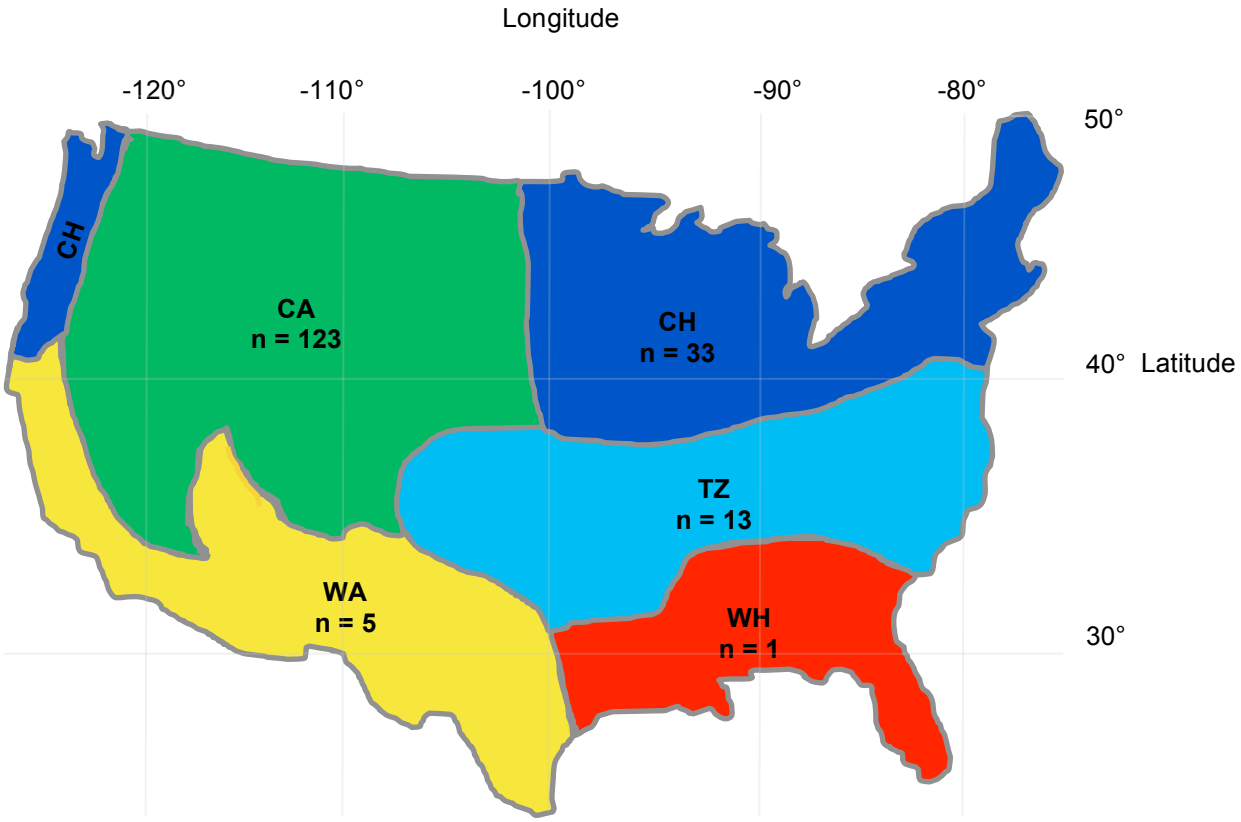

Figure 9. Red Angus sires assigned to five U.S. climates zones based broadly upon Köppen-Geiger climate classifications (Peel et al., 2007; CA = Cool Arid; CH = Cool Humid; TZ = Transition Zone; WA = Warm Arid; and WH = Warm Humid).

No phenotypic information was gathered on the Red Angus sires for the present study; however, the EPD and accuracy for eight growth and carcass traits are presented in Table 9. The average EPD accuracy of these traits was 0.75 ± 0.51 (accessed 3/17/2016). To achieve an accuracy of 0.56 for a moderately heritable trait, approximately 53 progeny records must be obtained for each sire (Greiner, 2013). Therefore, more than 10,440 progeny were potentially represented in these data.

Table 9. Eight growth and carcass traits and their corresponding expected progeny differences (EPD) and accuracies for 174 Red Angus sires used in the 2,000 Bull Project assigned to four climate zones. Data obtained from Red Angus Association of America (accessed 3/17/2016).

Trait	Cool Arid EPD	Cool Humid EPD	Transition Zone EPD	Warm Arid EPD	Average Accuracy
Birth Weight	-1.87	-0.45	-1.12	0.58	0.8768
Weaning Weight	55.71	63.47	64.55	59.00	0.8630
Yearling Weight	84.67	97.59	97.91	88.20	0.8629
Calving Ease Direct	6.46	3.03	3.82	2.60	0.8352
Calving Ease Maternal	4.94	3.63	2.73	3.60	0.8299
Marbling	0.45	0.43	0.63	0.46	0.5885
Rib-eye Area	0.03	0.00	0.00	0.39	0.5567
Fat	0.00	0.00	0.01	-0.01	0.5871

Analyses

Genetic Structure and Allele Frequency

Genetic structure of Red Angus sires was evaluated with ADMIXTURE 1.3 and the 13,960 SNP previously obtained. Ten runs were repeated for each value of *K* from 1 through 10. The estimated error observed with each *K* was used to determine the minimal number of clusters necessary to best explain the variation found in the analyzed samples.

A population genetics analysis was performed using the 66 SNP previously associated with traits influenced by climate. Red Angus sires assigned to climate zones were evaluated genotypically at each of the 66 loci for Hardy-Weinberg Equilibrium (HWE) and detection of loci (DLS) under selection using ARLEQUIN (Peakall and Smouse, 2012; Excoffier and Lischer, 2010). The HWE locus-by-locus test was performed using 1,000,000 Markov chain steps and 10,000 dememorization steps. The DLS analysis was performed with 100 simulated demes and 50,000 coalescent simulations. The SNP considered significant ($P < 0.05$) in the HWE and DLS analyses

were further evaluated for genetic differentiation through an analysis of molecular variance (AMOVA) using ARELQUIN with 10,000 permutations for significance and 1,000 permutations for Mantel test (Excoffier and Lischer, 2010). In addition, a population pairwise matrix based on Wright's Fixation Index (F_{ST}) that estimates the genetic distances between populations was constructed (Wright, 1951). Figure 10 describes the SNP-based analyses of Red Angus sires.

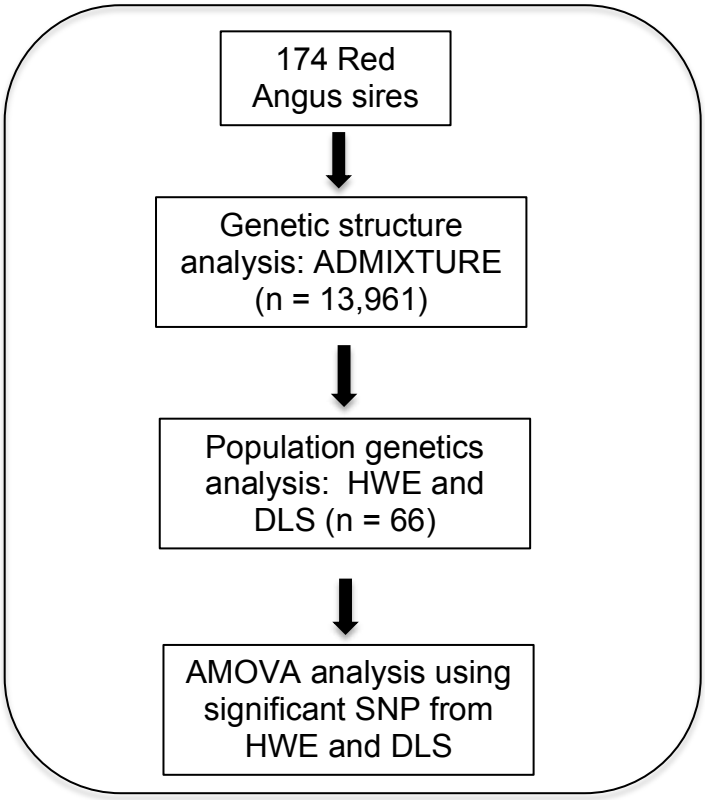

Figure 10. Description of SNP analyses used to evaluate Red Angus sires (n = 174) assigned to five U.S. climate zones.

Results

Fine-genetic structure analysis performed with 13,960 SNP and the ADMIXTURE software revealed that there were eight populations present in the 174 Red Angus sires (Fig. 11, Alexander et al., 2009). Although genetic structure was detected, clusters did not reflect an association to climate zones as shown in Hereford cattle in Chapter 3. However, clusters 1, 2, and 3 were in decreasing proportions across CA, CH, and TZ climate zones. Cluster 1 had large proportional assignment from WA climate zones (~38%). Cluster 4 had large proportional assignment from CH and WA climate zones at 23% and 26%, respectively. Clusters 5 and 6 were more predominant in the TZ climate zone, where the other climate zones had approximately 10% proportional assignment from clusters 5 and less than 8% proportional assignment from cluster 6. Cluster 7 was more prevalent in CA and WA climate zones at 9% and 6%, respectively. Lastly, the largest proportional assignment of cluster 8 was in the CH climate zone.

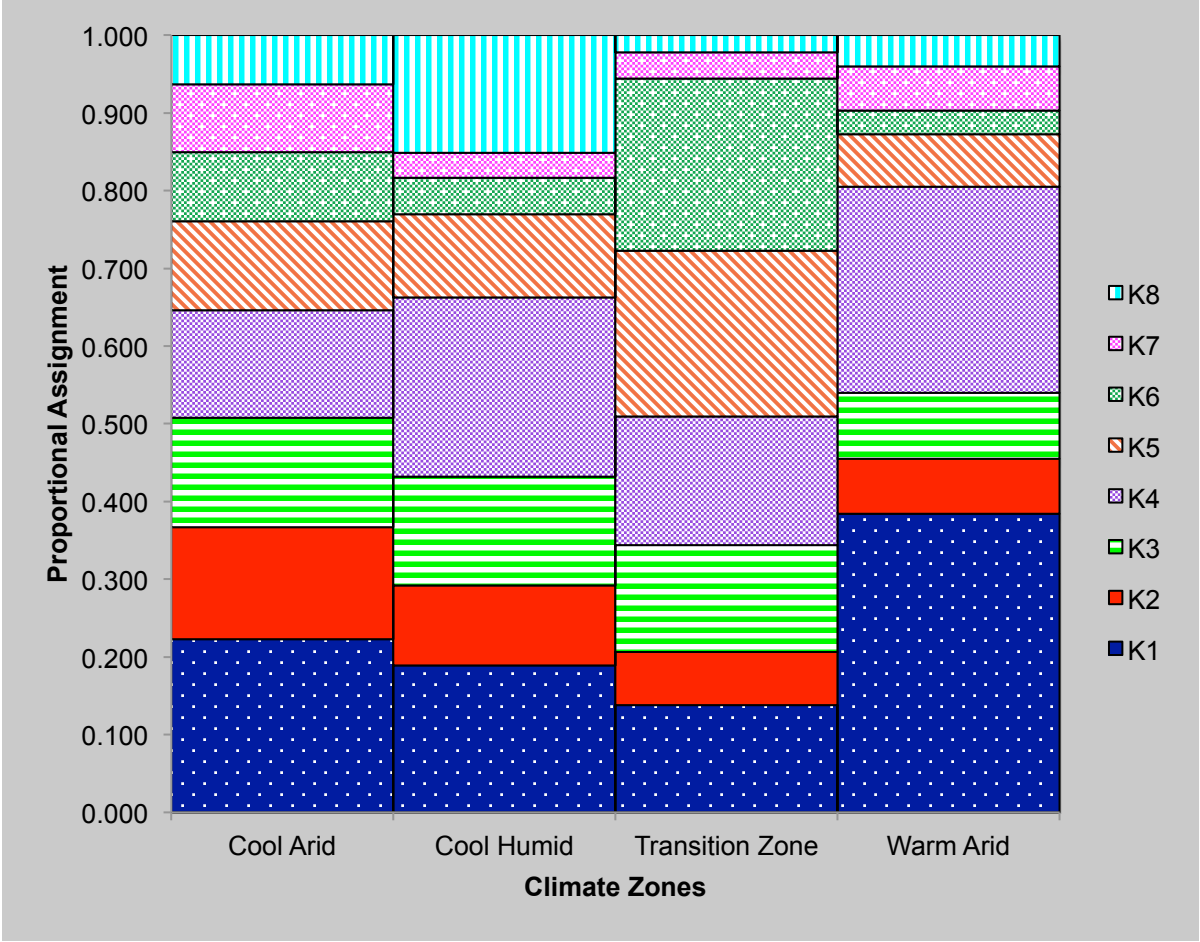

Figure 11. ADMIXTURE assignment of eight clusters of 174 Red Angus cattle based upon 13,960 SNP. The K value represents the proportion of the population detected.

Table 8 presented the coefficients of genetic relationships between Red Angus groups. The CA and WA zones had the lowest relationship with 0.07. Additionally, study of the 66 SNP potentially influenced by climate evaluated in the prominent Red Angus AI sires revealed that 23 SNP deviated significantly from HWE or DLS analyses across the climatic zones. These results were used to construct a population pairwise matrix and suggested no significant differences between the TZ and CA and WA climate zones (Table 10). Furthermore, low differentiation was observed between CA and CH, CA and TZ, and CH and TZ climate zones. There was moderate differentiation between CA and WA and CH and WA climate zones as indicated by the F_{ST} values. The highest differentiation (i.e., 0.10453) occurred between the CH and WA climate zones. Table 11 represents the expected and observed heterozygosity for the Red Angus cattle at the 66 loci. The observed heterozygosity levels for Red Angus sires were similar or higher than the heterozygosity levels observed in Hereford cattle in Chapter 3, but lower than the average heterozygosity of the 13,960 SNP panel of 0.352 ± 0.0011.

The 23 SNP that were significant for HWE and DLS were analyzed using AMOVA (Table 12). Seven of the 23 SNP were significant ($P < 0.05$) in these analyses associated with the traits of milk yield, early embryonic survival, and mature cow body. The number of SNP were 5, 1 and 1, respectively (Fig. 12). Based on the seven SNP, allele frequencies of the WA zone were dissimilar from the other climate zones for mature cow body weight and early embryonic survival. Allele frequencies of the CH zone were intermediate for most milk yield SNP. Although marginal allele frequency differences existed among climate zones, the SNP frequencies did not appear unique to

each climate zone based on the 66 SNP panel. Conversely, the ADMIXTURE analysis using 13,960 SNP revealed eight genetic subpopulations within the Red Angus breed.

Eight of the 66 SNP violated HWE and DLS for Red Angus and Hereford cattle (Fig. 13). Single-nucleotide polymorphism MY: rs109421300 (*Bos taurus* autosomal 14) was the only locus with relatively the same allele frequencies in both Hereford and Red Angus cattle. The other loci appeared to have diverse frequencies between the two breeds.

Table 10. Average population differentiation (F_{st}) of 23 SNP in Red Angus sires (n = 174) across U.S. climate zones.

	Region			
Region	Cool Arid	Cool Humid	Transition Zone	Warm Arid
Cool Arid	0.00000			
Cool Humid	0.02561*	0.00000		
Transition Zone	0.01135	0.03731*	0.00000	
Warm Arid	0.06876*	0.10453*	0.04408	0.00000

*$P < 0.05$

Table 11. Expected and observed heterozygosity in Red Angus sires (n = 174) assigned to four U.S. climate zones using 66 SNP.

Region	Number of cattle	Observed Heterozygosity	Expected Heterozygosity
Cool Arid	127	0.329	0.326
Cool Humid	32	0.347	0.333
Transition Zone	10	0.337	0.322
Warm Arid	5	0.333	0.292

Table 12. Analysis of molecular variance of 23 SNP significant for Hardy-Weinberg Equilibrium and detection of loci under selection in 174 Red Angus sires assigned to four U.S. climate zones (MY = Milk Yield; BW = Body Weight; HS = Heat Stress; HCR = Heifer Conception Rate; EES: Early Embryonic Survival)

SNP	Fst value	P-value
BW: rs110421124	0.0392	0.0415*
EES: rs42397090	0.0960	0.0007*
HCR: rs109262355	0.0159	0.1355
HS: rs43719996	0.0095	0.1874
HS: rs109890402	-0.0130	0.8155
HS: rs110209659	0.0192	0.1032
HS: rs42393904	-0.0111	0.7172
HS: rs109279094	-0.0058	0.5949
MY: rs110236070	0.1327	< 0.0001*
MY: rs110856800	0.0532	0.0053*
MY: rs109350371	-0.0049	0.3566
MY: rs109557202	0.0101	0.2110
MY: rs109421300	-0.0088	0.6918
MY: rs41627764	0.0735	0.0055*
MY: rs41581068	0.0076	0.1876
MY: rs108971409	0.1327	0.0002*
MY: rs41597129	-0.0083	0.6416
MY: rs42215845	0.0010	0.3561
MY: rs111008794	-0.0027	0.5834
MY: rs41613557	-0.0138	1.0000
MY: rs41635833	0.0908	0.0199*
MY: UA-IFASA-6228	0.0016	0.3263
MY: UA-IFASA-6878	-0.0142	0.9218

*Loci significant for AMOVA analysis: $P < 0.05$

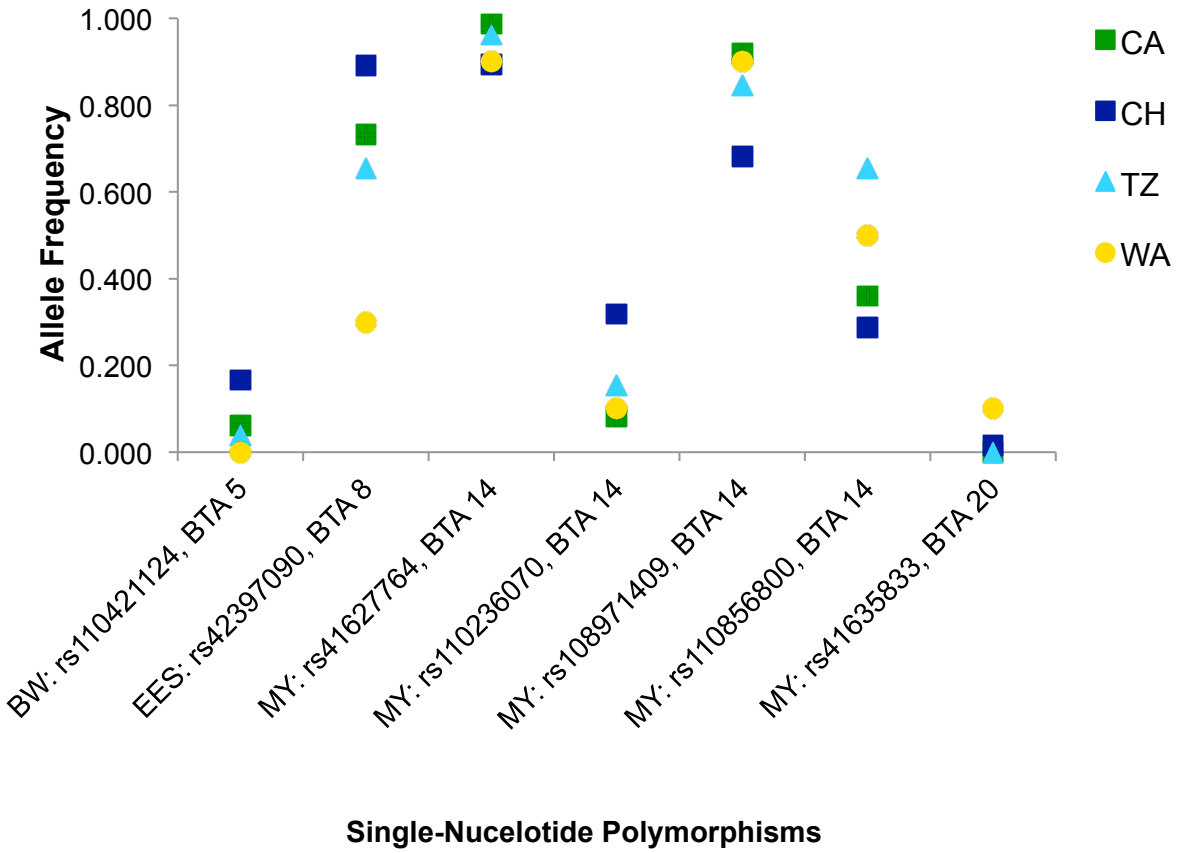

Figure 12. Frequencies of the "A" allele (genotypes in A/B format) in prominent Red Angus AI sires (n = 174) for SNP significant via AMOVA comparisons ($P < 0.05$). The x-axis represents trait, single-nucleotide polymorphism reference ID, and chromosome number. (BTA = *Bos taurus* autosomal; MY = Milk Yield; BW = Body Weight; HS = Heat Stress; CA = Cool Arid; CH = Cool Humid; TZ = Transition Zone; WA = Warm Arid; and WH = Warm Humid).

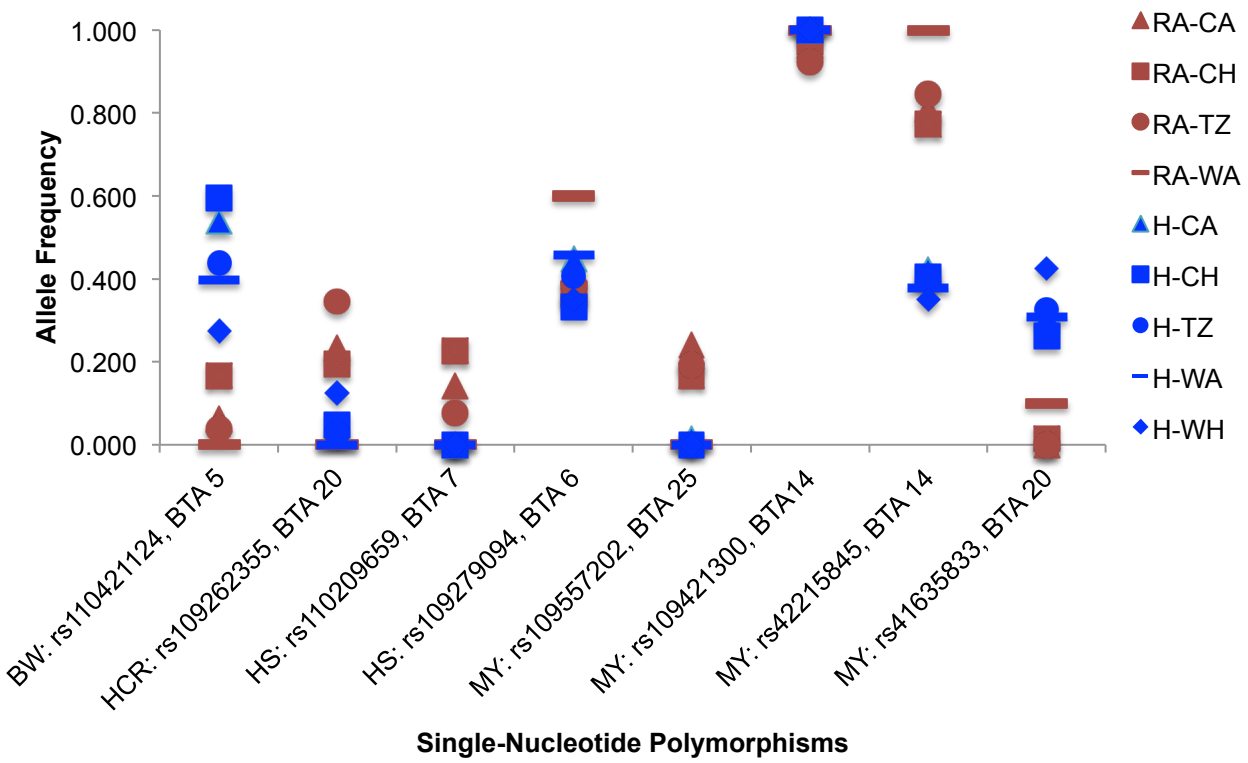

Figure 13. Frequencies of the "A" allele (genotypes in A/B format) for SNP (n = 8) that violated Hardy-Weinberg Equilibrium or detection of loci under selection for Red Angus (i.e., RA-CA) and Hereford (i.e., H-CA) cattle. The x-axis represents trait, single-nucleotide polymorphism reference ID, and chromosome number. (BTA = *Bos taurus* autosomal; HCR: Heifer Concept Rate; MY = Milk Yield; BW = Body Weight; HS = Heat Stress; CA = Cool Arid; CH = Cool Humid; TZ = Transition Zone; WA = Warm Arid; and WH = Warm Humid).

Discussion

Neutral genetic structure using 13,960 SNP revealed eight subpopulations within the Red Angus breed. However, the allele frequency analysis of SNP known to be associated with production traits likely influenced by climate did not reveal genetic substructure that corresponded with the U.S. climate zones in the Red Angus sires from the 2,000 Bull Project. However, as indicated by the significant F_{ST} values, Table 10 showed differentiation among the climate zones. The highest differentiation occurred between CH and WA climate zones. A similar result was observed in Chapter 3, and

supports the argument that arid and humid environments may require different physiological-genetic mechanisms of adaptation.

Although Red Angus genetic substructure did not correspond to the U.S. climate zones, the ADMIXTURE analysis of 174 Red Angus sires revealed distinct populations within the breed as shown in Fig. 14. This could have been due to the uneven sample size among climate zones (i.e. 70% of the predominant AI sires were assigned to the CA climate zone). Additionally, these data contained sires with lineages from Beckton Julian GG B571 (registration number 387580), which has been used by a large portion of Red Angus breeders (personal communication, Larry Keenan, RAAA, 2016). Beckton Julian GG B571 is not as prominent across the breed as the Line 1 pedigree in Hereford cattle (Leesburg, 2012), therefore, was not removed from the data. However, the predominance of AI sires in the CA climate zone, and the use of the Julian pedigree may have influenced the genetic structure that was observed within the breed. Nonetheless, more sampling is needed in WA and WH populations for the Red Angus breed.

Based on the ADMIXTURE analysis and the 23 SNP that violated HWE and DLS, the Red Angus breed has been subjected to either artificial or natural selection, which showed the genetic variability potential to respond to selection in differing environments. Additionally, the observed heterozygosity surpassed the expected level of heterozygosity for each climate zone using the 66 SNP associated with traits potentially influenced by climate. Furthermore, the observed level of heterozygosity for Red Angus cattle at the 66 SNP was similar to the observed level of heterozygosity for

Hereford cattle in Chapter 3. Therefore, it appears that Red Angus contain genetic diversity that would allow selection of favorable genotypes in various climates.

Figure 13 presented allele frequency differences between the Red Angus and Hereford breeds. Fig. 13 also suggested that there may be differences in selection presssures that are occurring among the two breeds. For example, the allele frequencies were similar between breeds for two of the eight SNP evaluated. For the other six SNP, allele frequency differences between the breeds ranged from .0167 to 0.428, 0.168 to 0.428, and 0.077 to 0.501 for CA, CH, and TZ regions, respectively. This is interesting, given the fact that these British *Bos taurus* breeds are heavily utilized for beef production in the U.S. In fact, the Hereford breed was the second most popular breed with 75,988 cattle registered in 2015, and Red Angus was the fourth most registered breed in the U.S. with 58,059 cattle registered in 2015 (AHA, 2016; RAAA, 2016). It should also be noted that population substructure exist among breeds even though these cattle breeds follow guidelines of the Beef Improvement Federation (2016) as to promote uniform data collection.

Red Angus AI rates were similar to Hereford; approximately 30% of calves born in 2015 were the results of AI (personal communication with Larry Keenan, RAAA; 2016). The modest AI rate could have influenced the genetic substructure that was identified in Hereford and Red Angus breeds and may suggest that regional breeding strategies are utilized by breeders. Hence, the genetic structure observed within Hereford and Red Angus breeds could be due to uniqueness of the sires and segregation of that animal's genetics throughout a region rather than regional climate adaptation.

In comparison to the Hereford coefficients of relationships, the Red Angus breed had lower coefficients of relationships with the exception of the WA zone (i.e. the climate zone with five sires). This finding suggests that based on climate zones the animals were assigned, the Hereford population overall has a higher relationships with one another in comparison to Red Angus.

Multiple factors may influence the genetic differences between the two breeds. For example, the American Hereford Association was formed in 1881 (AHA, 2016). In 1953, Hereford cattle registrations peaked in the U.S. at 560,794 head. At that time, the Red Angus Association of American had not been formed. The Red Angus Association of America was established in the U.S. in 1954 (RAAA, 2016). Unlike the Hereford breed, the Red Angus Association of America has not registered more than 60,000 head of cattle in any year (RAAA, 2016). Although registration numbers between the two breeds are similar today, the Hereford breed has historically had substantially more animals than the Red Angus breed. The historical difference in the number of cattle and the time-frame in which these two breeds have resided in the U.S. may provide explanation why the Red Angus sire's allele frequencies did not show genetic substructure that corresponded with climate zone and appeared most prevalent in the northwestern region of the U.S. (i.e., the location where the breed originated).

The Red Angus and Hereford allele frequencies may have differed because of differences in selection that has occurred historically within the two breeds. For example, the Angus breed (i.e., derived from Aberdeen, Scotland) has a black coat color. However, the red coat color in Red Angus cattle was derived from a frameshift mutation in the melanocyte-stimulating hormone receptor gene (Klungland et al., 1995).

Therefore, to produce red colored offspring in Angus, the sire and dam must contain the red recessive allele. The selection for animals that contain the mutated melanocyte-stimulating hormone receptor gene in the Red Angus breed may have altered the genepool from which the breed derived given the fact that the red coat color is recessive in the population. Although Hereford cattle are also red, they possess other color pattern alleles, such as white spotting (Seo et al., 2007). Therefore, their coat color selection did not rely strictly on one allele.

For the present study, methods were not taken to decrease familial-relatedness across climate zones for Red Angus sires as was executed in study of Hereford cattle in Chapter 3. Nonetheless, as climates continue to change, hardy animals that balance production and fitness-related traits are needed to sustain production (Knap, 2005) and genetic variation can aid with that objective. Based on the results and genotypes from the bulls studied in the 2,000 Bull Project, we reject our hypothesis that Red Angus bulls possess genetic substructure that corresponds to U.S. climate zones. However, genetic structure was observed within the breed, possibly due to the uneven sampling within climate zones. Additionally, based on the eight SNP that violated HWE and DLS for Red Angus and Hereford breeds, Red Angus sires allele frequencies differed from the Hereford cattle allele frequencies, suggesting different selection pressures within the two breeds.

Conclusion

Genetic structure appeared in Red Angus sires, but did not correspond with U.S. climate zones. Red Angus sires studied in the 2,000 Bull Project were concentrated in cool climates. This may be a result of the origin of Red Angus cattle in the northwestern

region of the U.S. or breeder preference for Red Angus cattle in this region. The uneven distribution of Red Angus sires to the CA region could be masking climate zone substructure that was observed in the Hereford data.

SUPPLEMENTARY MATERIAL

Introduction

The genetic structure of Hereford cattle in Chapter 3 was analyzed using an alternative method. This investigation was performed to determine if there were similarities or differences between the methods used to determine genetic structure.

Materials and Methods

Similar climate zones, cattle (n =278; pedigree relationships not accounted for) and genotypic data from Chapter 3 were evaluated. However, Hereford cattle were assigned to a climate zone based on GENALEX population assignment. This method utilized the 66 SNP loci potentially influenced by climate to assign animals to one of the five climate zones based upon the log likelihood of the expected genotype frequency at each locus for each respective population (Peakall and Smouse, 2012).

Validation of the climate zone assignment was performed. The genetic structure analysis was performed with 14,312 neutral SNP previously obtained and the STRUCTURE software (Pritchard et al., 2000). The analysis was executed with a 2,000 iteration burn in, 14,000 MCMC iterations, and K values from 1 to 9. All K values were replicated three times. The graphs were plotted using the best K repetition selected (Evanno et al., 2005).

Chapter 3 utilized ADMIXTURE 1.3 to determine the genetic structure of Hereford cattle. STRUCTURE and ADMIXTURE 1.3 are similar software packages in that they identify genetic structure within a population. STRUCTURE uses a Bayesian iterative method in which populations are designated to a population based upon individuals who share similar patterns of variation (Porras-Hurtado et al., 2013).

STRUCTURE uses a Markov Chain Monte Carlo (MCMC) estimation. ADMIXTURE 1.3 is computationally faster than STRUCTURE due to its numerical optimization algorithm (Alexander et al., 2009). One of the disadvantages of using ADMIXTURE is that it does not explicitly account for linkage disequilibrium (Porras-Hurtado et al., 2013).

Results

The heterozygosity for the 66 SNP associated with traits potentially influenced by climate in Hereford cattle are presented in Table 13.

Table 13. Assignment of animals and heterozygosity for Hereford cattle assigned to five U.S. climate zones (n = 278).

Climate Zone	Number of cattle	Heterozygosity
Cool Arid	45	0.354
Cool Humid	48	0.340
Transition Zone	76	0.357
Warm Arid	68	0.358
Warm Humid	41	0.357

Neutral genetic structure analysis performed with 14,312 SNP using STRUCTURE confirmed the validity of the five climate zones (Evanno et al., 2005). These analyses revealed that the WA zone appeared distinct, while the CA and CH zones had a high proportional assignment to K-3, the third population. The TZ had high levels of admixture and had intermediate proportional assignments for all K (Fig. 14 and 15).

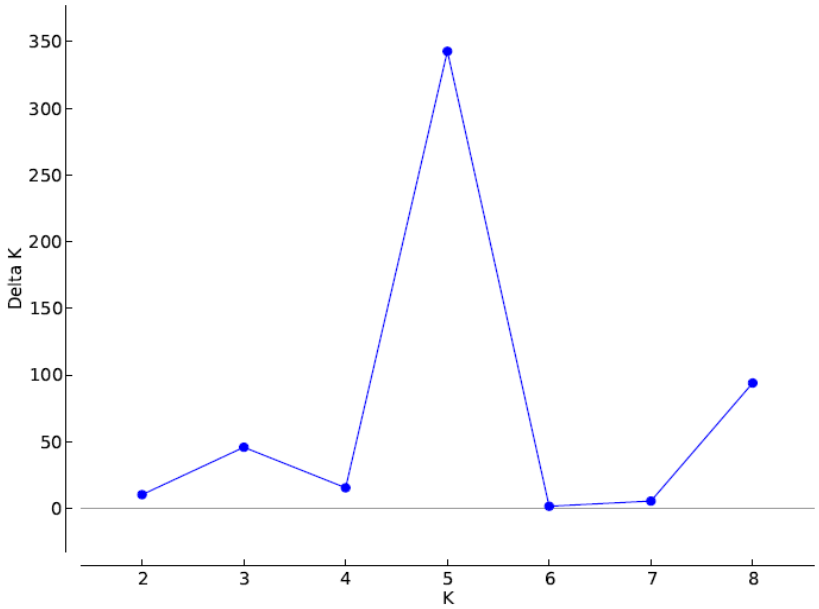

Figure 14. Plot of Delta K analysis using 14,312 SNP genotypes from 278 Hereford cattle confirming five U.S. climate zones.

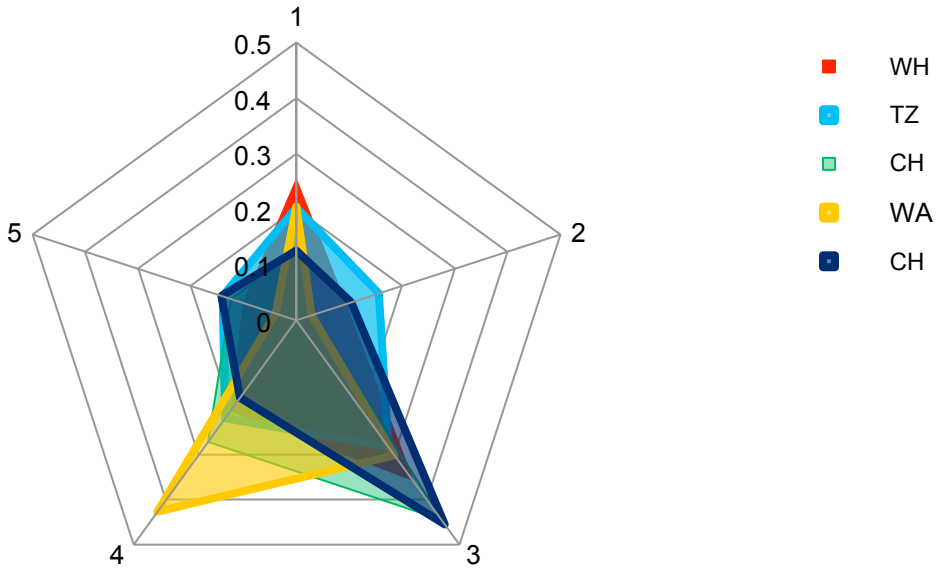

Figure 15. Proportional assignments (0.0 to 0.5) of Herefords sires (n = 278) into five populations by STRUCTURE. The axes represent the five separate populations within climate zones confirmed by the Delta K analysis. (CA = Cool Arid; CH = Cool Humid; TZ = Transition Zone; WA = Warm Arid; and WH = Warm Humid).

Population genetics evaluation using ARLEQUIN found that 25 SNP of the 66 SNP studied were not in HWE and (or) were under DLS. Pairwise F_{st} were calculated for regions using the 25 loci (Table 14) and revealed these subpopulations to be significantly different with the exception of the CA and TZ. Additionally, F_{st} values for CA and WH, CH and WH, TZ and WH indicated low differentiation, whereas there was moderate differentiation between CA and CH, CA and WA, CH and TZ, CH and WA, TZ and WA, TZ and WH, and WA and WH regions. Additionally, the 25 SNP which violated HWE or under DLS were evaluated using AMOVA (Table 12). Ten of the 25 SNP were significant ($P < 0.05$) via AMOVA comparison and their allele frequencies are presented in Fig. 16. Warm Arid and WH subpopulations appeared to be at opposite extremes, especially for SNP associated with heat stress, while TZ, CA, and CH were found to be intermediate. Figure 6 demonstrates the genetic substructure of the climate zones in the evaluated SNP.

Table 14. Average F_{st} values for Hereford cattle (n = 278) between five U.S. climatic zones.

	Climate Zone				
Climate Zone	[1]Cool Arid	Cool Humid	Transition Zone	Warm Arid	Warm Humid
Cool Arid	0.00000				
Cool Humid	0.06374*	0.00000			
[1]Transition Zone	0.00482	0.06331*	0.00000		
Warm Arid	0.12205*	0.05816*	0.10525*	0.00000	
Warm Humid	0.03466*	0.02227*	0.04660*	0.11385*	0.00000

*P < 0.001

[1]Genetic similarities were detected for Transition Zone and Cool Arid zone based on SNP that violated HWE or under DLS (n = 25).

Table 15. List of SNP tested in AMOVA analysis. 10 SNP were significant. Loci MY: ARS-BFGL-NGS-4939 only had one allele, therefore, not tested in AMOVA analysis. (BW: Body weight; EES: Early Embryonic Survival; HS: Heat Stress; MY: Milk Yield; DPR: Daughter Pregnancy Rate)

SNP	F_{st}	P-value
BW: rs110059753	0.00345	0.9756
BW: rs110421124	0.07454	< 0.0001*
BW: rs110505759	0.00612	0.3167
EES: rs110464321	0.2399	0.0078*
HS: rs42042561	0.19019	< 0.0001*
HS: rs11020659	0.00273	0.4682
HS: rs41609304	0.01279	0.7429
HS: rs42609685	0.22537	< 0.0001*
HS: rs52761380	0.19145	< 0.0001*
HS: rs109279094	0.06202	< 0.0001*
MY: rs110236070	0.04004	0.0010*
MY: rs110017379	0.01286	0.1085
MY: rs109968515	0.0057	0.2796
MY: rs109557202	0.00958	0.2014
MY: rs110529685	0.00215	0.5523
MY: rs110323635	0.1791	< 0.0001*
MY: rs41597129	0.00703	0.3236
MY: rs110199901	0.17406	< 0.0001*
MY: rs110060785	0.16559	< 0.0001*
MY: rs108995214	0.01219	0.1202
MY: rs52215845	0.01242	0.1222
MY: rs41635833	0.00786	0.2434
MY: rs110718625	0.00566	0.3490
DPR: rs41711496	-0.00116	0.8338

*Loci significant for AMOVA analysis: $P < 0.05$

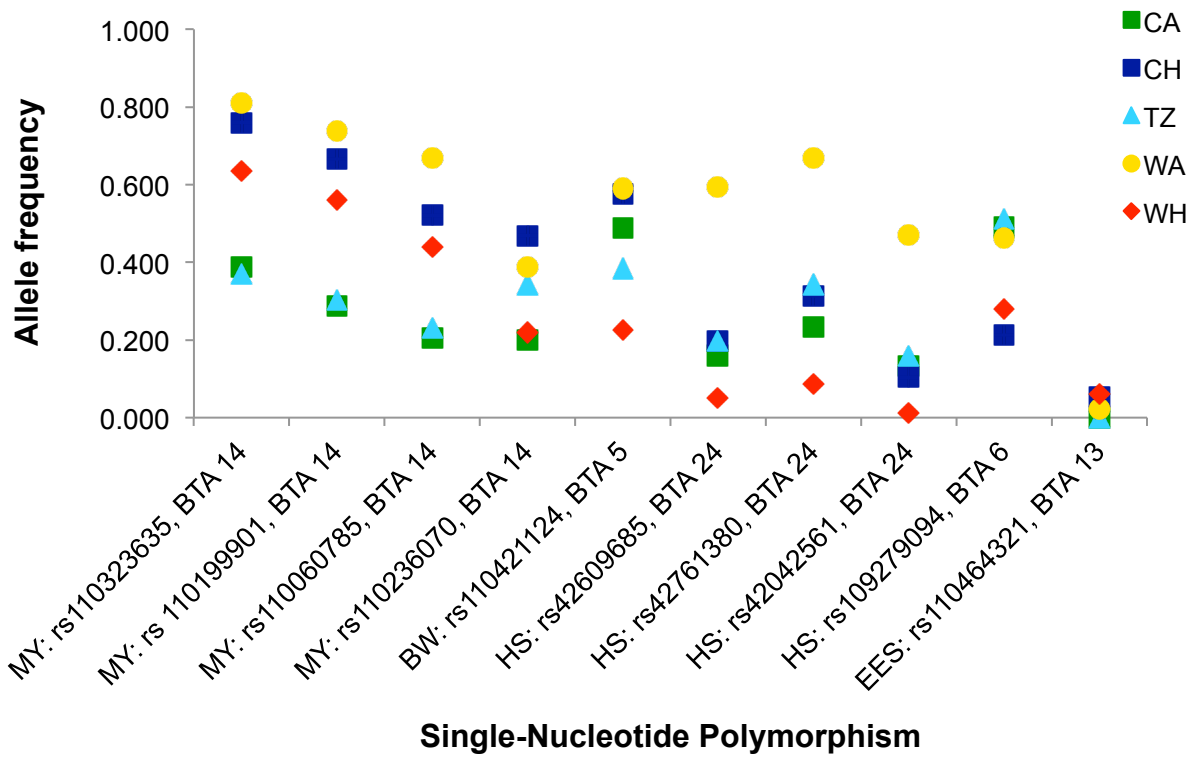

Figure 16. Frequencies of the A allele among five U.S. climate zones from loci that were significant in AMOVA comparisons (n = 10) in Population 1. The x-axis represents trait, single-nucleotide polymorphism reference ID, and chromosome number. (BTA = *Bos taurus* autosomal; MY = Milk Yield; BW = Body Weight; HS = Heat Stress; EES = Early Embryonic Survival; CA = Cool Arid; CH = Cool Humid; TZ = Transition Zone; WA = Warm Arid; and WH = Warm Humid).

The evaluation of Hereford cattle in Chapter 3 revealed 15 SNP that violated HWE and DLS analyses. The present Hereford evaluation revealed 25 SNP that violated HWE and DLS analyses. Ten common SNP violated HWE and DLS for the present Hereford analyses and the Hereford cattle evaluated in Chapter 3. The traits these 10 SNP represented were mature cow body weight (n = 1), heat stress (n = 4), and milk yield (n = 5). These SNP and their allele frequencies are presented in Fig. 17

and appeared similar for both populations (note, the overlap of HS:rs110209659, MY:rs109968515, MY: rs109557202, and MY:rs109421300 in the image).

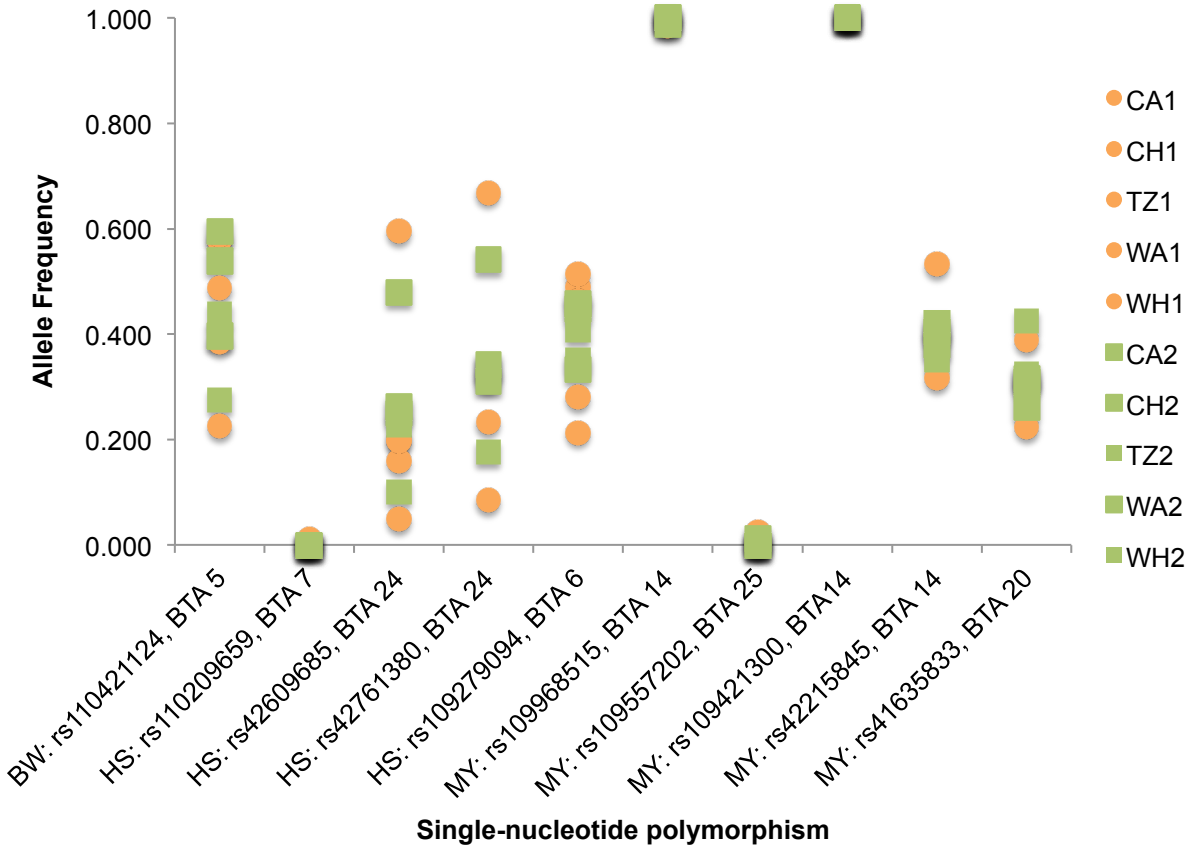

Figure 17. Single-nucleotide polymorphisms (n = 10) that violated HWE and DLS analyses for Hereford assigned to region based on breeder location (i.e. CA1) and Hereford assigned to climate region based on GENALEX population assignment (i.e. CA2). The x-axis represents trait, single-nucleotide polymorphism reference ID, and chromosome number. (BTA = *Bos taurus* autosomal; MY = Milk Yield; BW = Body Weight; HS = Heat Stress; CA = Cool Arid; CH = Cool Humid; TZ = Transition Zone; WA = Warm Arid; and WH = Warm Humid).

Discussion

Neutral genetic structure using 14,312 SNP and allele frequency analysis of SNP known to be associated with production traits likely influenced by climate revealed

Hereford cattle genetic substructure that corresponded with the U.S. climate zones. A similar analysis was performed with Hereford cattle in Chapter 3, however, the present study did not account for pedigree relationships, and the cattle were designated to climate zone based on the GENALEX population assignment.

Figure 16 revealed distinct genetic substructure for each climate zone, whereas as Chapter 3 Hereford cattle revealed apparent genetic structure in WA and WH climate zones. Ten SNP that were not in HWE or DLS for the present study and the Hereford study in Chapter 3 revealed allele frequency overlaps. However, allele frequency variation did appear in six of the ten SNP. Genetic structure analysis revealed five populations in the present study. This is different from the Chapter 3 results, where six clusters were present in the Hereford population.

Genetic substructure associated with climate zone was observed in Hereford cattle evaluated in Chapter 3, and the Hereford cattle in the present study. Although similar results were determined using different methods, variations between SNP allele frequencies and climate zone differentiation was observed.

REFERENCES

Adams, R. M., B. H. Hurd, S. Lenhart, and N. Leary. 1998. Effects of global climate change on agriculture: an interpretative review. Climate Res. 11:19-30.

AHA. 2016. Hereford History. http://hereford.org/node/47 (Accessed 23 March 2016).

AICA. 2016. History. http://charolaisusa.com/members/history.html (Accessed 27 August 2016).

Akdemir, D. 2014. Training population selection for (breeding value) prediction. arXiv preprint arXiv:1401.7953.

Alexander, D. H., J. Novembre, and K. Lange. 2009 Fast model-based estimation of ancestry in unrelated individuals. Genome Res. 19:1655-1664.

Agerholm, J. S., J. Arnbjerg, and O. Anderson. 2004. Familial chondrodysplasia in Holstein calves. J Vet Diag. Invest. 16:293-398.

Arguez, A., S. Applequist, R.S. Vose, I. Durre, M.F. Squires, and X. Yin. 2012. NOAA's 1981-2010 Climate normals: methodology of temperature-related normals. NCDC Report (7pp).

Bagnato, A. and A. Rosati. 2014. From the Editors-Animal selection: The genomics revolution. Anim. Front. 2:1-2.

Balding, D.J. 2006. A tutorial on statistical methods for population association studies. Nature Reviews Gen. 7:781-791.

Beaumont, M. A. and R.A. Nichols. 1996. Evaluating loci for use in the genetic analysis of population structure. Proc. Roy. Soc. London B: Biol. Sci. 263:1619-1626.

Bedwell, S. Personal Communication. August 31, 2016. American Hereford Association.

BIF. 2016. Across breed EPD adjustment factors. In: Proceedings. Manhattan, KS.

Boettcher, P. J., I. Hoffmann, R. Baumung, A. G. Drucker, C. McManus, P. Berg, A. Stell, L.B. Nilsen, D. Moran, M. Naves and M.C. Thompson. 2015. Genetic resources and genomics for adaptation of livestock to climate change. Front. Gen. 5:461-464.

Booy, G., J. J. Hendriks, M.J.M. Smulders, J.M. Van Groenendael, and B. Vosman. 2000. Genetic diversity and the survival of populations. Plant Biol. 2:379-395.

Bowman, J. C. 1972. Genotype x environment interactions. Ann. Gen. Sel. Anim. 4:117-123.

Braverman, J. M., R. H. Richard, N. L. Kaplan, C. H. Langley, and W. Stephan. 1995. The hitchhiking effect on the site frequency spectrum of DNA polymorphisms. Gen. 140:783-796.

Bohmanova, J., I. Misztal, and J. B. Cole. 2007. Temperature-humidity indices as indicators of milk production losses due to heat stress. J. Dairy Sci. 90:1947-1956.

Bouraoui, R., M. Lahmar, A. Majdoub, M. Djemali, and R. Belyea. 2002. The relationship of temperature-humidity index with milk production of dairy cows in a Mediterranean climate. Anim. Res. 51:479-491.

Burns, W. C., M. Koger, W. T. Butts, O. F. Pahnish, and R. L. Blackwell. 1979. Genotype by environment interaction in Hereford cattle: II. Birth and weaning traits. J. Anim. Sci. 49:403-409.

Butts, W.T., M. Koger, O.F. Pahnish, W.C. Burns, and E.J. Warwick. 1971. Performance of two lines of Hereford cattle in two environments. J. Anim. Sci. 33:923-932.

Cartwright, T. C. 1955. Responses of beef cattle to high ambient temperatures. J. Anim. Sci. 14:350-362.

Cavalli-Sforza, L. L. 1966. Population structure and human evolution. Proc. Royal Soc. London B:Biol. Sci. 164:362-379.

Chamberlain. A. J., B. J. Hayes, K. Savin, S. Bolormaa, H. C. McPartlan, P. J. Bowman, C. Van Der Jagt, S. MacEachern, M.E. Goddard. 2012. Validation of single nucleotide polymorphisms associated with milk production traits in dairy cattle. J Dairy Sci. 95:865-875. doi: 10.3168/jds.2010-3786.

Charlesworth, D. 2006. Balancing selection and its effects on sequences in nearby genome regions. PLoS Gen. 2:64-69.

Charlesworth, B. 2007. A hitch-hiking guide to the genome: a commentary on 'The hitch-hiking effect of a favourable gene' by John Maynard Smith and John Haigh. Genet. Res. 89:389-390.

Cleveland, M.A., H.D. Blackburn, R.M. Enns, and D.J. Garrick. 2005. Changes in inbreeding of US Herefords during the twentieth century. J. Anim. Sci. 83:992-1001.

Cochran, S. D., J. B. Cole, D. J. Null, P. J. Hansen. 2013. Discovery of single nucleotide polymorphisms in candidate genes associated with fertility and production traits in Holstein cattle. BMC Gen.14:49-72. doi:10.1186/1471-2156-14-49.

Cromie, A. R., D. L. Kelleher, F. J. Gordon, and M. Rath. 1999. Genotype by environment interaction for milk production traits in Holstein Friesian dairy cattle in Ireland. Interbull Bull.17:100-104.

Cundiff, L. V., R. M. Thallman, and L. A. Kuehn. 2012. Impact of Bos indicus genetics on the global Beef Industry. In: Beef Improvement Federation 44th Annual Research Symposium and Annual Meeting, Houston, T.X. 1-31.

Daetwyler, H. D., A. Capitan, H. Pausch, P. Stothard, R. van Binsbergen, R. F. Brondum, X. Liao, A. Djari, S. C. Rodriguez, C. Grohs, D. Esquerre, O. Bouchez, M. Rossignol, C. Klopp, D. Rocha, S. Fritz, A. Eggen, P.J. Bowman, D. Coote, A.J. Chamberlain, C. Anderson, C.P. VanTassell, I. Hulsegge, M.E. Goddard, B. Guldbrandtsen, M.S. Lund, RF. Veerkam, D.A. Boichard, R. Fries and B.J. Hayes. 2014. Whole-genome sequencing of 234 bulls facilitates mapping of monogenic and complex traits in cattle. Nat. Gen. 46:858-865.

Decker, J. E., J. C. Pires, G.C. Conant, S. D. McKay, M. P. Heaton, K. Chen, A. Cooper, J. Vilkki, C. M. Seabury, A. R. Caetano, and G. S. Johnson. 2009. Resolving the evolution of extant and extinct ruminants with high-throughput phylogenomics. Proc. Nat. Acad. of Sci. 106:18644-18649.

Delsuc, F., H. Brinkmann, and H. Philippe. 2005. Phylogenomics and the reconstruction of the tree of life. Nat. Rev. Genet. 6:361-375.

Den Boer, P.J., J. Szyszko, and R. Vermeulen. 1993. Spreading the risk of extinction by genetic diversity in populations of the carabid beetle Pterostichus oblongopunctuatus F. (Coleoptera, carabidae). Nether. J. Zoo. 43:242-259.

Devlin B., and N. Risch. 1995. A comparison of linkage disequilibrium measures for fine-scale mapping. Gen. 29:311-322.

Dikmen, S. and P. J. Hansen. 2009. Is the temperature-humidity index the best indicator of heat stress in lactating dairy cows in a subtropical environment? J. Dairy Sci. 92:109-116.

Dikmen, S., J. B. Cole, D. J. Null, and P. J. Hansen. 2013.Genome-wide association mapping for identification of quantitative trait loci for rectal temperature during heat stress in Holstein cattle. PLoS One 8:69202. doi:10.1371/journal/one.0069202.

de Jong, G. and P. Bijma. 2002. Selection and phenotypic plasticity in evolutionary biology and animal breeding. Livest. Prod. Sci. 78:195-214.

Eggen, A. 2012. The development and application of genomic selection as a new breeding program. Anim. Front. doi:10.2527/af.2011-0027.

Elsik, C. G., R. L. Tellam, and K. C. Worley. 2009. The genome sequence of taurine cattle: a window to ruminant biology and evolution. Sci. 324:522-528.

Evanno, G., S. Regnaut, and J. Goudet. 2005. Detecting the number of clusters of individuals using the software STRUCTURE: a simulation study. Mol. Eco. 14:2611-26200.

Excoffier, L., P.E. Smouse, J.M. and Quattro. 1992. Analysis of molecular variance inferred from metric distances among DNA haplotypes: application to human mitochondrial DNA restriction data. Genet. 131:479-491.

Excoffier, L. and H. E. L. Lischer. 2010. Arlequin suite ver 3.5: a new series of programs to perform populations genetics analyses under Linus and Windows. Mol. Eco. Res. 10:564-567.

Fussel, H. M. 2007. Adaptation planning for climate change: concepts, assessment approaches, and key lessons. Sus. Sci. 2:265-275.

Fischer, G., M. Shah, F. N. Tubiello, and H. van Velhuizen. 2005. Socio-economic and climate change impacts on agriculture: an integrated assessment, 1990-2080. Phil. Trans. R. Soc. 360:2067-2083.

Flori, L., S. Fritz, F. Jaffrézic, M. Boussaha, I. Gut, S. Heath, J. L. Foulley, and M. Gautier. 2009. The genome response to artificial selection: a case study in dairy cattle. PLoS ONE 4:6595. doi:10.1371/journal.pone.0006595.

García-Ruiz, A., J. B. Cole, P. M. VanRaden, G. R. Wiggans, F. J. Ruiz-López, and C. P. Van Tassell. 2016. Changes in genetic selection differentials and generation intervals in US Holstein dairy cattle as a result of genomic selection. Proc. Nat. Aca. Sci. 201519061.

Gaughan, J.B., Heat tolerance of Boron and Tuli crossbred steers. 1999. J. Anim. Sci. 77:2398-2405.

Gianola, D., H. Simianer, and S. Qanbari. 2010. A two-step method for detecting selection signatures using genetics markers. Gen. Res. Camb. 92:141-155.

Gibson, G., and I. Dworkin. 2004. Uncovering cryptic genetic variation. Nature Rev. Gen. 5:681-690.

Golden, B. L., D. J. Garrick, and L. L. Benyshek. 2009. Milestones in beef cattle genetic evaluation. J. Anim. Sci. 87:E3-E10.

Gouveia, J. J. S., M. V. G. Barbosa da Silva, S. R. Paiva, and S. M. Pinheiro de Oliveria. 2014. Identification of selection signatures in livestock species. Gen. Mol. Bio. 37:330-342.

Greiner, S.P. 2013. Genetic improvements from AI over natural service. Proc. App. Rep. Strategies in Beef Cattle Reproductive Strategies in Beef Cattle, Staunton, VA 209-212.

Guo, J., H. Jorjani, and Ö. Carlborg. 2012. A genome-wide association study using international breeding-evaluation data identifies major loci affecting production traits and stature in the Brown Swiss cattle breed. BMC Gen. 13:82-92. doi:10.1186/1471-2156-13-82.

Gutiérrez-Gil, B., J.J. Arranz, and P. Wiener. 2015. An interpretive review of selective sweep studies in Bos taurus cattle populations: identification of unique and shared selection signals across breeds. Front. Genet 6:167-187.

Hammond, A.C, T.A. Olson, C.C. Chase, Jr., E.J. Bowers, R.D. Randel, C.N. Murphy, D.W. Vogt, and A. Tewolde. 1996. Heat tolerance in two tropically adapted *Bos taurus* breeds, Senepol and Romosinuano, compared with Brahman, Angus, and Hereford Cattle in Florida. J. Anim. Sci. 74:295-303.

Hanotte, O., Tawah, C.L., Bradley, D.G., Okomo, M., Verjee, Y., Ochieng, J. and Rege, J.E.O. 2000. Geographic distribution and frequency of a taurine *Bos taurus* and an indicine *Bos indicus* Y specific allele amongst sub-Saharan African cattle breeds. Mol. Eco. 9:387-396.

Harris, E.E. and D. Meyer. 2006. The molecular signature of selection underlying human adaptations. Year. Phys. Anthro. 49:59-130.

Hayes, B. J., P. J. Bowman, A. J. Chamberlain, K. S. Savin, C. P. van Tassell, T. S. Sonstegard, and M.E. Goddard. 2009. A validated genome wide association study to breed cattle adapted to an environment altered by climate change. PLOS ONE 4:6676 doi:10.1371.

Hayward, A.C., R. Tollenaere, J. Dalton-Morgan, and J. Batley. 2015. Molecular marker applications in plants. In: Plant Genotyping: Methods and Protocols. Springer Science and Business Media New York, p.13-27.

Hazel, L. N. and J. L. Lush. 1942. The efficiency of three methods of selection. J. Hered. 33:393-399.

Holderegger, R. and H. H. Wagner. 2008. Landscape Genetics. BioSci. 58:199-207.

Holsinger, K. E. and Weir, B. S. 2009. Genetics in geographically structured populations: defining, estimating and interpreting FST. Nat. Rev. Gen. 10:639-650.

Holter, J. B., J. W. West, and M. L McGilliard. 1997. Predicting ad libitum dry matter intake and yield of Holstein cows. J. Dairy. Sci. 80:2188-2199.

Hu, Zhi-Luang, C. A. Park, X. L. Wu, and J. M. Reecy. 2013. Animal QTLdb: an improved database tool for livestock animal QTL/association data dissemination in the post-genome era. Nucleic Acids Res. 41:871-879.

Huang, W., B. W. Kirkpatrick, G. J. M. Rosa, and H. Khatib. 2010. A genome-wide association study using selective DNA pooling identifies candidate markers for fertility in Holstein cattle. Anim. Gen. 41:570-578.

Hubisz, M. J., D. Falush, M. Stephens, and J. K. Pritchard. 2009. Mol. Eco. Res. 9:1322-1332.

Hussin, J., P. Nadeau, J. F. Lefebvre, and D. Labuda. 2010. Haplotype allelic classes for detecting ongoing positive selection. BMC Bioinformatics 11:65.

Ingraham, R. H., D. D. Gillette, and W. D. Wagner. 1974. Relationship of temperature and humidity to conception rate of Holstein cows in subtropical climate. Dep. Of Phys. And Pharm. 57:476-481.

IPCC, 2014: Climate Change 2014: Synthesis Report. Contribution of Working Groups I, II and III to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change [Core Writing Team, R.K. Pachauri and L.A. Meyer (eds.)]. IPCC, Geneva, Switzerland, p.151.

Jones, P.G., and P.K. Thornton. 2009. Croppers to livestock keepers: livelihood transitions to 2050 in Africa due to climate change. Environmental Sci. and Pol. 12:427-437.

Joost, S., A. Bonin, M.W. Bruford, L. Despres, C. Conord, G. Erhardt, and P. Taberlet. 2007. A spatial analysis method (SAM) to detect candidate loci for selection: towards a landscape genomics approach to adaptation. Mol. Eco. 16:3955-3969.

Keenan, L. Personal Communication. August 16, 2016. Red Angus Association of America.

Kijas, J. W., J. A. Lenstra, B. Hayes, S. Boitard, L. R. P. Neto, M. San Cristobal, B. Servin, R. McCulloch, V. Whan, K. Gietzen, and S. Paiva. 2012. Genome-wide analysis of the world's sheep breeds reveals high levels of historic mixture and strong recent selection. PLoS Biol. 10:1001258.

Kim, Y. and W. Stephan. 2002. Detecting a local signature of genetic hitchhiking along a recombining chromosome. Gen. 160:765-777.

Kim, Y. and R. Nielsen. 2004. Linkage disequilibrium as a signature of selective sweeps. Genetics 167:1513-1524.

Kitts, A. and S. Sherry. 2002. The Single Nucleotide Polymorphism Database (dbSNP) of Nucleotide Sequence Variation. In: McEntyre J, Ostell J, editors. The NCBI Handbook [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2002. Chapter 5. Available from: http://www.ncbi.nlm.nih.gov/books/NBK21088/

Klungland, H., D.I. Vage, L. Gomez-Raya, S. Adalsteinsson, and S. Lien. 1995. The role of melanocyte-stimulating hormone (MSH) receptor in bovine coat color determination. Mam. Gen. 6:636-639.

Knap, P.W. 2005. Breeding robust pigs. Australian J. of Exp. Ag. 45:763-773.

Krehbiel, B.C., M.G. Thomas, H.D. Blackburn, S.E. Speidel, R.M. Enns, and L. Keenan. 2016. Evaluation of genetic structure across five US climate zones using prominent AI sires of two British *Bos taurus* breeds. In WESTERN SECTION Amer. Soc. Anim. Sci. Meeting 88th Annual Meeting, Salt Lake City, UT, July 2016.

Krehbiel, B. C., S. Paiva, C. Wilson, S. Ericsson, J. Boatright, M.G. Thomas, and H.D. Blackburn. 2015. Untapped genetic variability in Herefords: Implications for climate change. In: WESTERN SECTION Amer. Soc. Anim. Sci. 87th Annual Meeting, Ruidoso, NM, June 2015.

Koger, M., W.C. Burns, O.F. Pahnish, and W.T. Butts. 1979. Genotype by environment interactions in Hereford cattle: I. Reproductive traits. J. Anim. Sci. 49:396-402.

Kopelman, N. M., J. Mayzel, M. Jakobsson, N.A. Rosenberg, and I. Mayrose. CLUMPAK: a program for identifying clustering modes and packaging population

structure inferences across K. Mol Ecol Resourc 2015: 15:1179-91. doi:10.1111/1755-0998.12387
Kreitman, M. 2000. Methods to detect selection in populations with applications to the human. Annu. Rev. Genomics Hum. Gen. 1:539-59.
Kuehn, L. A., J. W. Keele, G. L. Bennett, T. G. McDaneld, T. P. L. Smith, W.M. Snelling, T.S. Sonstegard, and R.M. Thallman. 2011 Predicting breed composition using breed frequencies of 50,000 markers from the US Meat Animal Research Center 2,000 Bull Project. Sci. Soc. 89:1742-1750.
Kuehn, L. A. and R. M. Thallman. 2012. Beef Improvement Federation. Houston, TX. www.beefimprovement.org/PDFs/2012/2012 BIFProceedings. p.152-177.
Lewontin, R.C., 1988. On measures of gametic disequilibrium. Genet. 120:849-852.
Laval, G., N. Iannuccelli, C. Legault, D. Milan, M. A. Groenen, E. Giuffra, L. Andersson, P. H. Nissen, C. B. Jorgensen, P. Beeckmann, and H. Geldermann. 2000. Genetic diversity of eleven European pig breeds. Gen. Sel. Evol. 32:187-204.
LCI. 1970. Patterns of Transit Losses. Livestock Conservation, Inc., Omaha, NE.
Lutz, W. and Samir, K.C. 2010. Dimensions of global population projections: what do we know about future population trends and structures? Phil. Trans. Roy. Soc. London B:Biol. Sci. 365:2779-2791.
Leesburg, V.L.R. 2012. The influence of Line 1 Herefords on the global Hereford population (Doctoral dissertation, University of the Free State).
Lillehammer, M., B.J. Hayes, T.H.E. Meuwissen, and M.E. Goddard. 2009. Gene by environment interactions for production traits in Australian dairy cattle. J. Dairy Sci. 92:4008-4017.
Lin, B. Z., Sasazaki, S. and Mannen, H., 2010. Genetic diversity and structure in *Bos taurus* and *Bos indicus* populations analyzed by SNP markers. J. Anim. Sci. 81:281-289.
Lôbo, R. B., Nkrumah, D., Grossi, D. D. A., De Barros, P. S., Paiva, P., Bezerra, L. A. F., De Oliveira, H.N. and Da Silva, M.V.B., 2011. Implementation of DNA markers to produce genomically-enhanced EPDs in Nellore cattle. Acta Scientiae Veterinariae 39:s23-s27.
Lv, Feng-Hua, S. Agha, J. Kantanen, L. Colli, S. Stucki, J.W. Kijas, S. Joost, Meng-Hua Li, and P.A Marsan. 2014. Adaptations to climate-mediated selective pressures in sheep. Mol. Biol. Evol. 31:3324-3343.
MacNeil, M. D., M.A. Cronin, H. D. Blackburn, C. M. Richards, D. R. Lockwood and L. J. Alexander. 2007. Genetic relationships between feral cattle from Chirikof Island, Alaska and other breeds. International Soc. Anim. Gen. Animal Gen. 38:193-197.
Madalena, F. E., 2005. June. Considerations on the management of animal genetic resources in Latin America. In Proc. of EAAP/SLU/FAO/ICAR Workshop on “Sustainable Management of Animal Genetic Resources: Linking perspectives globally”, Uppsala, Sweden p.10.
Mader, T. L. 2002. Environmental stress in confined beef cattle. Amer. Soc. Agron. 81:E110-E119.
Manel, S. and R. Holderegger. 2013. Ten years of landscape genetics. Tren. Eco. Evol. 28:614-621.
Marlowe, T. J., 1964. Evidence of selection for the snorter dwarf gene in cattle. J. Anim. Sci. 23:454-460.

Mason, I. L., 1969. A world dictionary of livestock breeds, types and varieties. Technical Communications. Commonwealth Bureau of Animal Breeding and Genetics, 8.

Matukumalli, L. K., C. T. Lawley, R. D. Schnabel, J. F. Taylor, M. F. Allan, M. P. Heaton, J. O'Connell, S. S. Moore, T. P. Smith, T. S. Sonstegard, and C.P. Van Tassell. 2009. Development and characterization of a high density SNP genotyping assay for cattle. PLoS ONE 4:e5350. doi:10.1371/journal.pone.0005350.

Maxa, J, M. Neuditschko, I. Russ, M. Förster, and I. Medugorac. 2012. Genome-wide association mapping of milk production traits in Braunvieh cattle. J. Dairy Sci. 95:5357-5364. doi:10.3168/jds.2011-4673.

McTavish, E. J. and D. M. Hillis. 2014. A genomic approach for distinguishing between recent and ancient admixture as applied to cattle. J. Hered. 105:445-456.

McVean, G. 2007. The structure of linkage disequilibrium around a selective sweep. Genet. 175:1395-1406.

Mekonnen, M.M. and A.Y. Hoekstra. 2010. The green, blue and grey water footprint of farm animals and animal products. Val. Wat. Res. Report.

Menne, M., I. Durre, B. G. Gleason, T. G. Houston, and R. S. Vose, 2012: An overview of the Global Historical Climatology Network-Daily database. J. Atmos. Oc. Tech. 29:897-910, doi:10.1175/JTECH-D-11-00103.1h**.**

Meredith, B.K., F.J. Kearney, E.K. Finlay, D.G. Bradley, A.G. Fahey, D.P. Berry, D.J. Lynn. 2012. Genome-wide associations for milk production and somatic cell score in Holstein-Friesian cattle in Ireland. BMC Gen. 13:1-11. doi: 10.1186/1471-2156-13-21.

Meuwissen, T., B. Hayes, and M. Goddard. 2016. Genomic selection: A paradigm shift in animal breeding. Anim. Front. doi: 10.2527/af.2016-0002.

Montgelard, C., S. Zenboudji, A. Ferchaud, V. Arnal, and B.J. van Vuuren. 2012. Landscape genetics in mammals. Mammalia. 78:139-157.

Mulder, H. A., R. F. Veerkamp, B. J. Ducro, J. A. M. van Arendonk, and P. Bijma. 2006. Optimization of dairy cattle breeding programs for different environments with genotype by Environment Interaction. J. Dairy Sci. 89:1740-1752.

Muir, W. M., G. Wong, Y. Zhang, J. Wang, M. A. Groenen, R. P. Crooijmans, H. J. Megens, J. Zhang, R. Okimoto, A. Vereijken, A. Jungerius, G. A. A. Albers, C. T. Lawley, M. E. Delany, S. MacEachern, and H. H. Cheng. 2008. Genome-wide assement of worldwide chicken SNP genetic diversity indicates significant absence of rare alleles in commerical breeds. Proc. Nat. Aca. Sci. 105:17312-17317.

Napel, J., M. P. L. Calus, H. A. Mulder, and R. F. Veerkamp. 2009. Genetic concepts to improve robustness in dairy cows. In: M. Klopcic, R. Reents, J. Philipsson, and A. Kuipers, editors, Breeding for robustness in cattle. Wageningen Academic Publishers. The Netherlands. p.35-44.

Nardone, A., B. Ronchi, N. Lacetera, M.S. Ranieri, and U. Bernabucci. 2010. Effects of climate changes on animal production and sustainability of livestock systems. Livestock Sci. 130:57-69.

Nidup, K. and C. Moran. 2011. Genetic diversity of domestic pigs as revealed by microsatellites: A mini review. Gen. Quant. Gen. 2:5-18.

Nishimura, S., T. Watanabe, K. Mizoshita, K. Tatsuda, T. Fujita, N. Watanabe, Y. Sugimoto, and A. Takasuga. 2012. Genome-wide association study identified three major QTL for carcass weight including the PLAG1-CHCHD7 QTN for stature in Japanese black cattle. BMC Gen. 13:40-51.

Notter, D. R. 1999. The importance of genetic diversity in livestock populations of the future. J. of Anim. Sci. 77:61-69.

O'Brien, S. J. and R. Stanyon. 1999. Phylogenomics: Ancestral primate viewed. Nat. 402:365-366.

Omernik, J. M. and G. E. Griffith. 2014. Ecoregions of the conterminous United States: evolution of a hierarchical spatial framework. Envi. Man. 54:1249-1266.

Paaby, A. B. and M. V. Rockman. 2014. Cryptic genetic variation: evolution's hidden substrate. Nat. Rev. Gen. 15:247-258.

Pahnish, O.F., Koger, M., Urick, J.J., Burns, W.C., Butts, W.T. and Richardson, G.V., 1983. Genotype× Environment Interaction in Hereford Cattle: III. Postweaning Traits of Heifers. J. Anim. Sci. 56:1039-1046.

Pan, D., S. Zhang, J. Jiang, L. Jiang, Q. Zhang, and J. Liu. 2013. Genome-wide detection of selective signature in Chinese Holstein. PLoS ONE 8:e60440. doi:10.1371/journal.pone.0060440.

Parry, M., N. Arnell, T. McMichael, R. Nicholls, P. Martens, S. Kovats, M. Livermore, C. Rosenzweig, A. Iglesias and G. Fischer. 2001. Millions at risk: defining critical climate change threats and targets. Global Environ. Chan. 11:181-183.

Peakall, R. and P.E. Smouse. 2012. GENALEX 6.5: genetic analysis in excel. Population genetic software for teaching and research-an update. Bio. 28:2537-2539.

Peel, M. C., B. L. Finlayson, and T. A. McMahon. 2007. Updated world map of the Köppen-Geiger climate classification. Hydrology and earth system sciences disc. 4:439-473.

Porras-Hurtado, L., Y. Ruiz, C. Santos, C. Phillips, Á. Carracedo and M. Lareu. 2013. An overview of STRUCTURE: applications, parameter settings, and supporting software. Front. Gen. 4:98-112

Pritchard, J. K., M. Stephens, and P. Donnelly. 2000. Inference of population structure using multilocus genotype data. Gen. 155:945–959.

Purfield, D.C., D.P. Berry, S. McParland, D.G. Bradley. 2012. Runs of homozygosity and population history in cattle. BMC Gen. 13:70-81.

Qanbari, S. and H. Simianer. Mapping signatures of positive selection in the genome of livestock. 2014. Livest. Sci. 166:133-143.

RAAA. 2016. The history of Red Angus. http://assets.redangus.org/media/Documents/Association/Red_Angus_History_Brochure.pdf (Accessed 23 March 2016).

Raffrenato, E., R. W. Blake, P. A. Oltenacu, J. Carvalheira, and G. Licitra. 2003. Genotype by environment interaction for yield and somatic cell score with alternative environmental definitions. J. Dairy Sci. 86:2470-2479.

Robinson, M. R., A. J. Wilson, J. G. Pilkington, T. H. Clutton-Brock, J.M. Pemberton and L.E.B. Kruuk. 2009. The impact of environmental heterogeneity on genetic architecture in a wild population of Soay sheep. Gen. 181:1639-1648.

Saatchi, M., R. D. Schnabel, J. F. Taylor, D. J. Garrick. 2014. Large-effect pleiotropic or closely linked QTL segregate within and across ten US cattle breeds. BMC Genomics 15:442-458 doi: 10.1186/1471-2164-15-442.

Sabeti, P.C., P. Varilly, B. Fry, J. Lohmueller, E. Hostetter, C. Cotsapas, X. Xie, E.H. Byrne, S.A. McCaroll, R. Gaudet, S.F. Schaffner, E.S. Lander, and The International HapMap Consortium. 2007. Genome-wide detection and characterization of positive selection in human populations. Nat. 449:913-918.

Sabeti, P. C. S. F. Schaffner, B. Fry, J. Lohmueller, P. Varilly, O. Shamovsky. A Palma, T.S. Mikkelsen, D. Altshuler, and E.S. Lander. 2006. Positive Natural Selection in the Human Lineage. Sci. 312:1614-1620.

Sabeti, P. C., D. E. Reich, J.M. Higgins, H. Z. Levine, D. J. Richter, S. F. Schaffner, S. B. Gabriel, J. V. Platko, N. J. Patterson, G. J. McDonald, and H. C. Ackerman. 2002. Detecting recent positive selection in the human genome from haplotype structure. Nat. 419:832-837.

Seo, K., Mohanty, T.R., Choi, T. and Hwang, I., 2007. Biology of epidermal and hair pigmentation in cattle: a mini-review. Vet. Derm. 18:392-400.

Star, L., E. D. Ellen, K. Uitdehaag, and F. W. A. Brom. 2007. A plea to implement robustness into a breeding goal: poultry as an example. J. Ag. Environ. Eth. 21:109-125.

Seo, K., Mohanty, T.R., Choi, T. and Hwang, I., 2007. Biology of epidermal and hair pigmentation in cattle: a mini-review. Vet. Derm. 18:392-400.

Storfer, A., M. A. Murphy, J. S. Evans, C. S. Goldberg, S. Robinson, S. F. Spear, R. Dezzani, E. Delmelle, L. Vierling, and L.P. Waits. 2007. Putting the 'landscape' in landscape genetics. Hered. 98:128-142.

Segelbacher, G., S. A. Cushman, B. K. Epperson, M. Fortin, O. Francois, O.J. Hardy, R. Holderegger, P. Taberlet, L. P. Waits, and S. Manel. 2010. Applications of landscape genetics in conservation biology: concepts and challenges. Conserv. Gen. 11:375-385. doi: 10.1007/s10592-009-0044-5.

Senft, R.L. and L.R. Rittenhouse. 1985. A Model of Thermal Acclimation in Cattle. J. Anim. Sci. 61:297-306.

Shoville, S.D., A. Bonin, O. Francois, S. Lobreaux, C. Melodelima, and S. Manel. 2012. Adaptive genetic variation on the landscape: methods and cases. Annu. Rev. Ecol. Evol. Syst. 43:23-43.

Slatkin, M. 1987. Gene flow and geographic structure of natural populations. Sci. 236:787-792.

Thornton, P.K., J. van de Steeg, A. Notenbaert, and M. Herrero. 2009. The impacts of climate change on livestock and livestock systems in developing countries: A review of what we know and what we need to know. Agric. Sys. 101:113-127.

Thuy, N. T. D., E. Melchinger-Wild, A. W. Kuss, N. V. Cuong, H. Bartenschlager, and H. Geldermann. 2006. Comparison of Vietnamese and European pig breeds using microsatellites. J. Anim. Sci. 84:2601-2608.

Van Vleck, L.D., L.V. Cundiff, T. L. Wheeler, S. D. Shackelford, and M. Koohmaraie, 2007. Across-breed adjustment factors for expected progeny differences for carcass traits. J. Anim. Sci. 85:1369-1376.

Voight B. F., S. Kudaravalli, X. Wen, and J. K. Pritchard. 2006. A map of recent positive selection in the human genome. PloS Biol. 4:446-458.

West, J. W. 2003. Effects of heat-Stress on production in dairy cattle. J. Dairy Sci. 86:2131-2144.
Weng, Z., H. Su, M. Saatchi, J. Lee, M. G. Thomas, J. R. Dunkelberger, and D. J. Garrick. 2016. Genome-wide association study of growth and body composition traits in Brangus beef cattle. Livest. Sci. 183:4-11.
Willham, R.L. 1982. Genetic improvement of beef cattle in the United States: cattle, people and their interaction. J. Anim. Sci. 54:659-666.
Wolfgang, L. and K.C. Samir. 2010. Dimensions of global population projections: what do we know about future population trends and structures? Phil. Trans. Royal Soc. London B:Biological Sci. 365:2779-2791.
Wright, S., 1922. Coefficients of inbreeding and relationship. Amer. Nat. 56:330-338.
Wright, S. 1950. Genetical structure of populations. Nat. 166:247-49.
Wright, S. 1951. The genetical structure of populations. Ann. Eug. 15:323–354.
Wright, S. 1965. The interpretation of population structure by F-statistics with special regard to systems of mating. Evol. 395-420.
Ye, X., S. Avendano, J. C. Dekkers, and S. J. Lamont. 2006. Association of twelve immune-related genes with performance of three broiler lines in two different hygiene environments. Poultry Sci. 85:1555-1569.
Zhou, S., S. Goldstein, M. Place, M. Bechner, D. Patino, K. Potamousis, P. Ravindran, L. Pape, G. Rincon, J. Hernandez-Ortiz, and J.F. Medrano. 2015. A clone-free, single molecule map of the domestic cow (*Bos taurus*) genome. BMC Genomics, 16:644-663.
Zwald, N. R., K. A. Weigel, W. F. Fikse, and R. Rekaya. 2003. Identification of factors that cause genotype by environment interaction between herds of Holstein cattle in seventeen countries. J. Dairy Sci. 86:1009-1018.