Review on Status of Selection for Heat Tolerance Improvement in Cattle

Tassew Mohammed

Department of Animal Science, College of Agriculture, Woldia University, Mersa, Ethiopia.
Correspondence: tassewm010@gmail.com

ABSTRACT

The objective is to review the status of selection for heat tolerance improvement in cattle. Economic losses due to heat stress have been significant. Heat stress occurs when THI greater than the animal's thermo-neutral zone. Many strategies were suggested and implemented to mitigate heat stress. Among them, breeding for improved heat tolerance could be taken as a cost effective and long term solution of the problem. Animal breeding have showed rapid and appreciable advancement. Nowadays, quantitative based breeding has been complemented with molecular based breeding. Identification of heat tolerant cows could help to improve dairy performance through genetic selection. Several measures have been proposed as criteria to identify heat tolerant animals. Differences in thermal tolerance exist among cattle provide clues to select thermo-tolerant animals using genetic tools. The heritability of rectal temperatures under heat stress conditions in cattle ranged from 0.13 to 0.17. There is also heat shock gene related to thermo-tolerance that was identified and being used as marker in marker assisted selection and genome-wide selection to develop thermo-tolerant breeding bull. Heat tolerance genomic breeding values were developed for Holstein and Jersey bulls with reliability of heat tolerance of 30%. Breeding strategies to improve heat tolerance depend on the production system. The genetic mechanisms of heat-stress sensitive and tolerance should be identified before trying to improve heat resistance in dairy cows and in order to optimize the animal breeding program, it is important to add molecular genetic techniques along with the conventional animal breeding methods.

Keywords: Selection, Gene, Cattle, Heat tolerance, Heat Stress, Improvement

INTRODUCTION

Heat stress is one of the serious problems of livestock agriculture in tropical and sub-tropical countries. Economic losses due to heat stress have been significant. In the United States of America (USA), about 45%-60% of the losses occurred in the dairy industry [$897 million] whereas 20% ($369 million), 15% and 7% of losses were reported in beef, pig and poultry industries (Bernabucci *et al.*, 2010; Prathap *et al.*, 2017). Heat stress occurs when any combination of environmental factors cause the effective temperature of the environment to be higher than the animal's thermo-neutral zone and the animal then face difficulty to dissipate the heat and undergoes stress (Armstrong, 1994). The negative influence of heat stress on the performance and life of animal may become devastating if it is not managed well. Many strategies were suggested and implemented to mitigate heat stress (Armstrong 1994, Silanikove 2000, Chandra *et al.*, 2015, Amaral-Phillips, 2016). Among them, breeding for improvement of heat tolerance could be taken as a cost effective and long term solution of the problem. Animal breeding have showed rapid and appreciable advancement. Nowadays, it has started shifting from quantitative based to molecular based breeding. During last three decades, developments in DNA technologies have made it possible via uncovering a large number of genetic polymorphisms at the DNA sequence level and to use them as markers for evaluation of the genetic basis for observed phenotypic variability and makes a vital part in animal breeding. The use of molecular techniques could help to solve some of the limitations such as inefficiency for traits that are difficult to measure, have a low heritability, express late in the life of animals and sex limited (Garner *et al*., 2016; Nguyen *et al*., 2017; María *et al*., 2019). Also, the traditional selection within populations has not been very efficient when the selection objective involves several characteristics with unfavorable genetic correlation, for example, milk production and protein content of milk (Schwerin *et al*., 1995). Hence, in order to optimize the animal breeding program, it is important to add molecular genetic techniques along with the conventional animal breeding methods

An indicator of heat stress is temperature humidity index (THI). Once THI reaches 68 units and above, physiological changes arise which compromise fertility and milk production (Prathap *et al*., 2017; Chen *et al*., 2018). Efforts was undertaking to improve reproductive performance in cattle include the application of DNA technologies to discover novel molecular markers associated with thermo-tolerance in animals managed under warm environments. Identification of heat tolerant cows through genetic selection could help to improve dairy performance (West, 2003). But Collier *et al*. (2008) suggested that the genetic mechanisms of heat-stress sensitivity and tolerance should be identified before trying to improve heat resistance in dairy cows. The heat sensitivity and tolerance of animal is dependent on its genetic adaptation. Hotter climate adapted animals have heat shock protein, and slick genes. The Heat shock protein genes (Hspg) function as molecular chaperones that help animals to cope with heat stress by protecting the cells whereas the slick genes regulate body temperatures during heat stress. In heat tolerance, genotype by environment interaction is also important. Hotter climate adapted better perform in the lowland areas than cold climate adapted animals, vis-versa. Overall, it is the genetic component of the animals that determine the sensitivity and tolerance of heat stress.

In order to increase genetic gain of selection for fertility traits in dairy cows managed under a harsh environment, an effective strategy may be to use Single Nucleotide Polymorphism (SNP) genotypes from specific genes involved in reproduction. Genotypes from such genes could be used to construct molecular breeding values (MBV) for genetic prediction of reproductive traits. Prolactin and growth-insulin-like growth factor 1 (GH-IGF1) pathways involve several genes associated with thermo-tolerance and fertility in dairy cattle. However the different studies done in different research centers and universities about the current trend of genetic selection and breeding for heat tolerance improvement in cattle have not been adequately reviewed and published. The review provided information on the: genes involved in thermo tolerances in cattle, criteria that help to identify thermo-tolerant cattle, current achievements of thermo tolerance cattle production and breeding strategies for improved heat tolerance in cattle. Therefore, the objective is to review the status of selection for heat tolerance improvement in cattle.

Breeding for Improvement of Heat Tolerance

Heat stress (HS) is an ongoing concern in many livestock production sectors, including the dairy industry in many countries. Heat-stressed cows reduce feed intake and as a consequence producing less milk (St-Pierre *et al*., 2003). Heat stress is also known to impact health and reproductive performance of dairy cows (Schuller *et al*., 2014; Das *et al*., 2016). Therefore, there is a need to select for a more heat-tolerant population of dairy cows to be able to adapt to such changes. This will enable a long term, permanent and cumulative solution to improve dairy cow heat tolerance. Compared to traditional breeding, genomic selection is well suited to select for heat tolerance as it enables faster rates of genetic gain, as individuals can be selected very early in life. Genetic evaluation efforts were made to select heat-tolerant animals by analyzing of performance under heat stress. These efforts were successful on dairy cattle (Bohmanova *et al*., 2005) and beef cattle (Bradford *et al*., 2016). A genome wide enhanced evaluation was also developed to estimate genetic merit for heat-tolerance in dairy cattle in Australia (Nguyen *et al*., 2016).

Breeding Advancement

During the last five decades, the application of methods based on population genetics and statistics allowed the development of animals with a high productive efficiency. The basis is predicting the breeding values of the animals using phenotypic and genealogical information. Properties of the predictions are equivalent to the levels of correlated random effects of a mixed linear model or best linear unbiased predictors (BLUP) which is based to a large extent on the work of Henderson (1984). Now days, the use of molecular techniques could help to solve some of the limitations of the current methods. Molecular techniques allow detecting variation or polymorphisms exists among individuals in the population for specific regions of the DNA. These polymorphisms can be used to build up genetic maps and to evaluate differences between markers in the expression of particular traits in a family that might indicate a direct effect of these differences in terms of genetic determination on the trait (Albert *et al*., 1994, Lewin, 1994, Stein *et al*., 1996). These days, highly variable and effective molecular markers have been used to study heat tolerance or sensitivity of cattle at genome wide level. In this regard, Single Nucleotide Polymorphisms (SNPs) chips (bovine chips) are available in the National Centre for Biotechnology Information (NCBI), Gene Bank and DNA Data Base of Japan (DDBJ). Generally, breeding of livestock has depended upon Quantitative Genetics and Best Linear Unbiased Prediction (BLUP) up to 1990 whereas Quantitative Trait Loci (QTL) and marker assisted selection up to 2007 and Genomic selection (a decade year ago to onwards). Breeding is more advanced in temperate countries. The Asia countries have been also using molecular techniques as a complementary to conventional breeding to improve livestock. In Australia, genomic breeding value of heat tolerance was developed and used for Jersey and Holstein bulls. Similarly, dairy cattle having rich slick genes, such as Slick-Gator Fiona calf, Senepol Cattle Bull, and Slick-Gator Lone Ranger bull, are being produced in USA.

Responses of Cattle to Heat Stress

The level of heat stress can be measured by an animal's response to climatic conditions. Climatic conditions can be described by a combination of environmental factors such as air temperature, solar radiation, relative humidity, and wind speed. However, the temperature humidity index (THI) combines dry bulb temperature and relative humidity is a popular measure of levels of heat stress (Bohmanova *et al*., 2007). When temperatures increase above the thermo neutral zone, it trigger a chain of physiological, an atomical and behavioral changes in the animal's body, such as reduction of feed intake, decline of performance (milk production, growth, and reproduction), decrease of activity, increase of respiratory rate and body temperature, increase of peripheral blood flow and sweating and change in endocrine function (Prathap *et al*., 2017).

Assessment Methods for Heat Stress Tolerance

Different methods have been developed to identify heat tolerant animals. These included Rectal temperature (Trec) (Bianca, 1965, Igono and Johnson, 1990); Stress degree hours (Igono and Johnson, 1990); Milk temperature (West *et al*., 2003); Respiratory rate and heart rate (Bianca, 1965), Ear skin temperature and Skin temperature and Tympanic temperature (Hahn *et al*., 1999); Heat shock proteins (Hsps) (Hoffmann *et al*., 2003); diurnal patterns of temperature (night time cooling) (Kabuga, 1992).

Genetic Basis of Heat Tolerance

Adaptation is a change which reduces the physiological strain produced by a stressful component of the total environment. There are two types of adaptations namely genetic and phenotypic adaptations. Genetic adaptation is a genetically fixed condition of specie, which favors survival in a particular environment whereas phenotypic adaptation is an adaptation occurring within the lifetime of the organism. Acclimation, Acclimatization and hardening are some of phenotypic adaptation. Acclimation is a short term physiological change, occurring within the lifetime of an organism due to experimentally induced stressful changes, in particular, climatic factors, whilst acclimatization is a short term, usually seasonal, physiological change, occurring within the lifetime of an organism, caused by stressful changes in the natural climate (Yousef, 1985). Hardening is a short term process induced by extreme but non-lethal stress conditions. The changes brought about by hardening are reversible, whereas acclimation leads to irreversible changes. These changes affect fitness traits such as fecundity and longevity and stress resistance. Heat tolerance does have genetic basis. A study was performed on rectal temperature variations in dairy cows in Florida by Dikmen *et al*. (2012) and has found that rectal temperatures varied from 101.1 ^{0}F to 104.0 ^{0}F on a day when the dry-bulb temperature was 90 ^{0}F, showing that some cows are better at regulating their body temperatures than others and the heritability of rectal temperature under heat stress conditions ranged from 0.13 to 0.17 (Dikmen *et al*., 2012). This means that about 13-17% of the variation among cows in rectal temperature during heat stress is the result of variation in genetics. A good heritability value of 0.15 to 0.31 for rectal temperature was reported by Seath (1947). This value is relatively low compared to a trait like milk yield, where heritability is ~ 0.30 (Pritchard *et al*., 2013), but it is high enough to allow selection for rectal temperature under genomic selection index method.

Genes involved in Bovine Heat Stress Responses

Heat shock proteins (Hsps) function as molecular chaperones that help animals to cope with stress. They can be induced in addition to heat by environmental factors such as cold, heavy metals, ethanol fumes, insecticides, parasites, diseases or genetic stress (inbreeding). Hsps are primarily involved in protein quality system; they fold proteins and prevent aggregation of misfolded proteins (Sorensen *et al*., 2003). There is heat shock gene related to thermo tolerance that was identified and being used as marker in marker assisted selection and genome-wide selection to developed thermo tolerant bull that are used in breeding program. The heat shock genes are highly preserved and show low variation between species, suggesting evolutionary importance of cell protection during and after stress. Hsp expression is fine-tuned (not being only an on-off mechanism) and are also continuously expressed after a mild chronic stress exposure (Hoffmann *et al*., 2003). Major families of Hsps are Hsp100, Hsp90, Hsp70, Hsp60, Hsp40 and the small Hsps (so-called Hsps of sizes below 30 kDa). To date, research has been mainly focused on the Hsp70 family. The HSP70 protein, which is encoded by the HSP70A1A gene, is a widespread protein of the HSP family and an important intracellular molecular chaperone. The regulation of HSP70 production is critical to inhibit the apoptosis of cells (Mosser *et al*., 2000). The prospect of using the Hsp 70 family as a selection criterion for heat tolerance are widely considered in high input livestock production system. Another heat tolerant gene is Slick gene, which was first described in the Senepol breed of beef cattle that originated in the Virgin Islands, is a dominant gene that causes very short hair growth and regulate body temperatures during heat stress. The slick gene is caused by a mutation in the prolactin receptor gene (a gene involved in milk yield). The mutation is dominant – meaning inheritance of one copy of the gene leads to the offspring having short hair. The slick mutation arose naturally in several breeds of cattle in the Caribbean basin, including the Senepol, Carora, and Criollo Limonero.

Modeling Genetic Variability of Heat Tolerance

Genetic evaluation is prediction of the genomic breeding value (GEBV) of an animal for a single trait or multiple traits using phenotypic measurements and genotypes for a large number of markers spread throughout the genome. Heat tolerance (HT) can be defined as the rate of decline in milk, fat and protein yields per unit increase of THI. Most of the studies (Ravagnolo and Misztal, 2000; Garner *et al*., 2016;

Nguyen *et al*., 2017; María *et al*., 2019) designed to determine the genetic value of heat tolerance of animals have focused on modeling the genetic component of performance under high heat loads. This approach describes the genetic component of the reaction to heat stress in performance with the so-called broken line model. The broken line model is defined by two parameters: 1) the thermo neutrality threshold and 2) the slope of decay in production after passing this threshold as a consequence of heat stress (Bernabucci *et al*., 2014). Alternatively, Brügemann *et al*. (2011), Menendex-Buxadera *et al*. (2012), and Carabaño *et al*. (2014) proposed the use of polynomials of second or third order to describe the norm of reaction of milk production across the heat load scale. Polynomial functions provide a more flexible approach than broken line models and allow for a smoother transit from thermo tolerance to heat stress, instead of an abrupt change after the thermo neutrality threshold in broken line models (Santana *et al*., 2016). With this approach, steeper slopes at higher temperatures are accommodated, instead of a constant slope of decay in the broken line model, as might be expected to occur in reality. Reaction norm models using performance (both productive and reproductive) records and meteorological information have been extensively applied to measure heat tolerance in dairy or meat oriented production (Menéndez-Buxadera *et al*., 2012; Biffani *et al*., 2016; Bradford *et al*., 2016).

One of the main issues in the application of this approach is how to combine climate variables in the models to define the amount of heat load that is received by the animals. A number of studies have dealt with the use of alternative definitions of indices that combine temperature, humidity and additional meteorological variables such as wind speed or insulation (Gaughan *et al*., 2012). The definition of the lag between the date of recording the animal's performance and the date for which weather conditions better determine the subsequent animal's response in performance has the same importance as the weather variables to be included in a heat load index (Bernabucci *et al*., 2014, Carabaño *et al*., 2014, Ramón *et al*., 2016). Another important issue is to determine the selection criteria derived for each model. In the broken line model, both the thermo tolerance threshold and the slope of response of each individual could be used as selection criteria. However, the estimation of individual thresholds has been found to be troublesome from a computational point of view (Sánchez *et al*., 2009). Most applications of this model assign a predetermined value for the threshold and only the slope is estimated for each animal. The large estimated genetic correlation between threshold and slope [−0.95 in Sánchez *et al*. (2009)] indicates that selecting animals with less negative slope of response under heat stress will also result in higher thermo tolerance thresholds. When higher than first-order polynomials or other functions are used to describe the norm of reaction to heat stress, the definition of selection criteria is less obvious. Alternative selection criteria might be the slope of the individual polynomial curves under moderate or severe heat stress or principal component values derived from the Eigen decomposition of the covariance matrix of the random regression coefficients for the genetic component (Carabaño *et al*., 2014; Macciotta *et al*., 2017).

Selection indices with appropriate weighing for production and heat tolerance might be used to overcome the antagonistic relationship between those two traits. However, determining the appropriate economic weight for heat tolerance may be complex because of the difficulty of identifying all the animal performance parameters that are altered by heat stress and quantifying the associated economic loss.

Generally, up to now, the attempts to undertake genetic evaluations to select heat-tolerant animals have been made based on analyses of performance under heat stress. These attempts were performed for dairy (Bohmanova *et al*., 2005) and beef cattle (Bradford *et al*., 2016). More recently, a genome wide enhanced evaluation has been developed to estimate genetic merit for heat-tolerance in dairy cattle in Australia (Nguyen *et al*., 2016). This could be done by combining eleven years of weather station data, herd test day milk yields of 366,000 cows, and genomic data (632,003 SNP markers) and for each cow in the data set, the rate of decline in milk production with increasing THI was estimated. This heat tolerance phenotype was then used to derive genomic predictions for the trait. Australia HT GEBV was developed using 497 Holstein and 183 Jersey sires as validation populations (Nguyen *et al*., 2016) with a reliability of heat tolerance of 30% in both Holsteins and Jerseys. The HT average genetic breeding value (ABVg) ranged from 84 to 112 (−4 to +3 SD) in Holsteins and 86 to 117 (−3 to +4 SD) in Jerseys ((Nguyen *et al*., 2016)). In the most extreme sires, when the THI went from 60 to 90° F, daughters of the least heat-tolerant sires had a decrease in milk yield from about 40 to 28 lb/day (0.4 lb/THI unit). In contrary, daughters from the most heat-tolerant sire did not decrease milk production at all as the THI increased. The GBV was released to breeding company for propagation in 2017.

Advantages of Genomic Selection for Heat Tolerance

According to Nguyen *et al*. (2016), genomic selection for Heat Tolerance has many advantages. This will enable a long term, permanent and cumulative solution to improve dairy cow heat tolerance. It is cost effective. Compared to traditional breeding, genomic selection is well suited to select for heat tolerance as it enables faster rates of genetic gain, as individuals can be selected very early in life. Genomic selection for heat tolerance has an advantage that genotypes of thousands of cows and bulls are already available in Australia.

Challenges of Genomic Selection for Heat Tolerance

Challenges of Genomic Selection for Heat Tolerance are identified (Nguyen *et al*., 2016). The challenges are: (1) Genotype by environmental interaction (G*E) between thermal comfort and HS conditions exist (2) a genetic antagonism between HS tolerance and high milk production, (3) no extra costs to the existing milk recording schemes but has some disadvantages (4) current milk recording information does not seem to fully capture the productive response to high heat loads (5) the possible disadvantages of this type of selection, such as producing cows less resistant to cold stress or negative relationships between heat tolerance and other economically important traits.

Therefore, too overcome the disadvantages, the genetic correlation between heat tolerance with fertility and production traits must be investigated before heat tolerance is incorporated into selection criteria of dairy cattle.

Characteristics of Heat Tolerant Animals

In principle, a heat-tolerant animal is one that maintains homeothermy under high environmental heat loads. Maintaining homeothermy under hot conditions depends on the animal’s ability to balance thermogenesis and heat dissipation. Several measures have been proposed as criteria to identify heat tolerant animals; these include body temperature, respiration rate, heart rate, and sweating rate (Gray *et al*., 2011). In general, small animals have a thermoregulatory advantage over large animals because of their greater surface area per unit of body mass. For the same reason a slender animal with large body appendages, such as dewlap and ears, has an advantage over a compact animal with small appendages but otherwise similar features. The superiority of heat tolerance seems to be the result of a higher sweating rate and of lower heat production per unit body weight. Animals with low body temperature might have inherited low food intake and heat production regardless of the level of environmental heat stress (Brown and Downs, 2006; Glanville and Seebacher, 2010). In general, the metabolic rate of heat adapted animals is lower than animals of temperate regions. Heat loss is amplified by a greater surface area, particularly in the region of the dewlap and prepuce, a larger number of sweat glands, and short hair. Furthermore, lighter coat colors and the distribution of fat such as intramuscular or fat in the hump will assist in heat loss from the core (Yousef, 1985). More efficient metabolism and consequently lower heat production is one of the main characteristics of a heat tolerant animal (Bohmanova *et al*., 2005; Dikmen *et al*., 2014).

In a harsh environment more resources are required for fitness and health related traits than in an optimal environment. A heat tolerant cow which metabolizes nutrients more effectively has more resources for fitness, health, and reproduction, compared to her heat sensitive contemporaries. On this basis, it can be hypothesized that a heat tolerant cow is more resistant not only to heat stress but also to other stressors such as diseases, feed quality and quantity and parasites. In such a heat tolerant cow, improved fertility and fewer health problems can lead to a longer productive life. Studies done by on the immunological responses of a heat-tolerant (Romosinuano breed) and a heat sensitive-breed (Angus) demonstrated differences in metabolic response (i.e., immuno-resistance, hormone levels, etc.) between breeds under changes in ambient temperature, which may help understand differences in productivity among cattle breeds in response to heat stress. A less dense hair coat in the Romosinuano breed compared to the Angus, may play an important role in its ability to tolerate higher temperatures. The genetic variation for rectal temperature and hair coat density observed in these studies (Gray *et al*., 2011; Nguyen et al., 2016) suggests the future possibility of producing cows with greater heat tolerance from sires selected on genetic merit for this trait. Several biomarkers such as blood parameters (Van Goor *et al*., 2016) or diverse molecules associated with the heat stress response have also been proposed as indicators of heat stress in livestock (Min *et al*., 2017).

Breed Difference in heat tolerance

Slick gene is a dominant gene associated with very short hair growth, lighter coat color, an increased sweating rate, lower rectal temperature and lower respiration rate in homozygous cattle under hot conditions (Mariasegaram *et al.,* 2007). The gene is identified in Bos taurus tropical cattle (Senepol and Carona) (Figure 2). A beef cow of the Brahman or Nelore breed can maintain productivity in hot environments because it contains genes that allow animals to regulate body temperature during heat stress. There are also some dairy breeds like the Gir and dairy crosses, the Girolando are used in the tropics. Romosinuano breed and Angus demonstrated differences in metabolic response between breeds under changes in ambient temperature. Several reports showed associations of SNP in the Hsp genes with thermal stress response and tolerance in farm animals. Association of polymorphisms in Hsp90AB1 with heat tolerance has also been reported in Thai native cattle (Charoensook *et al*., 2012), and Sahiwal and Frieswal cattle (Deb *et al*., 2013) whereas HSF1 gene (Li *et al*., 2011), HSP70A1A gene (Li *et al*., 2011), HSBP1 (Wang *et al*., 2013) are associated heat tolerance in Chinese Holstein cattle. The non-Hsps genes also revealed to undergo changes in expression in response to HS. The ATP1B2 gene in Chinese Holstein cows (Wang *et al*., 2011) and ATP1A1 gene in Jersey crossbred cows (Das *et al*., 2016) was observed to have associated with thermo-tolerance. The indigenous tropical cattle have better heat tolerance capacities than the exotic cattle as they have evolved under stressful environmental condition for long generations. The heat tolerance capabilities have also genetic basis and acquired via natural and artificial selections.

Source: Dikmen **et al**. (2014)

Figure 1. A calf with the slick mutation (Slick-Gator Fiona)

Source: Dikmen *et al*. (2014)

Figure 2. Senepol Cattle Bull (left) and Slick-Gator Lone Ranger (right) with slick genes

Breeding Approaches for Heat Tolerance

About three breeding approaches for heat tolerance were suggested and used (María *et al*., 2016; Nguyen *et al*., 2017). (1) When the production system is sufficient to provide adequate feeding, management, heat mitigation, and controlled parasite and pathogenic environment, selection for heat tolerance within highly productive breeds is likely to offer far more opportunity than improving local breeds. (2) Crossing of local and selected breeds and then selection for productivity and monitoring of heat tolerance seems to be the 2nd best option to improve productivity in production systems that cannot provide mitigation for heat, adequate nutritional conditions or control of parasites and other pathogens. This method was applied in Holsteins in Mediterranean conditions (Carabaño *et al*., 2017) and Gyr in the tropics (Santana *et al*., 2015). For both populations, genetic selection to increase milk production has had an associated negative response in the animal's ability to cope with heat stress. Thus, even for locally adapted breeds, heat tolerance has to be monitored when selection for productivity is implemented in production systems affected by heat stress. (3) The third approach for improving resistance to heat stress in dairy breeds is to introduce thermo-tolerance genes from other breeds. One such gene is called the slick gene. This gene, which was first described in the Senepol breed of beef cattle that originated in the Virgin Islands, is a dominant gene that causes very short hair growth. The slick gene has been introduced naturally into some Holstein cows in Puerto Rico and into a dairy breed in Venezuela called the Carora (Olson *et al*., 2003, Dikmen *et al*., 2008). In addition, Tim Olson of the University of Florida used crossbreeding with Senepol and backcrossing to introduce the slick gene into Holstein cows in Florida and the resulting offspring were better able to regulate their body temperature during heat stress than cows with normal hair (Figure 1 & 2). Slick Holsteins are better able to regulate body temperature during heat stress than cows with normal hair (Dikmen *et al*., 2008). In Venezuela, Olson *et al*. (2003) found that Carora-Holstein crossbreds with the slick gene had lower rectal temperatures and higher milk yield than Carora-Holstein crossbreds with normal hair length.

CONCLUSIONS AND RECOMMENDATIONS

The negative influence of heat stress on the performance and life of animal may become devastating if it is not managed well. Economic losses due to heat stress have been also significant. There is considerable genetic variability in the response to heat stress in cattle that allows breeder to make selection for lower rectal temperature under heat stress. Continued selection for milk production will result in greater susceptibility to heat stress that realize a genetic antagonism between heat stress tolerance and high milk production. List of putative candidate regions and genes with known roles in heat tolerance has been identified. HT GEBVs were developed for Holstein and Jersey bulls with reliability of heat tolerance of 30%. Thermo-tolerant bull can be used in breeding program to have thermal adapted offspring. Physiological traits are the golden standard measure of heat tolerance. Breeding strategies to improve heat tolerance depend on the production system. The genetic mechanisms of heat-stress sensitive and tolerance should be identified before trying to improve the trait in dairy cows. Both climate and animal data should be collected and monitored for the detection of thermal stress situations. In order to optimize the animal breeding program, it is important to add molecular genetic techniques along with the traditional animal breeding methods.

REFERENCES

Albert, B., Bray, D., Lewis, J., Raff, M., Roberts, K. and Watson, J.D. 1994. Molecular biology of the cell. Garland Publishing, Inc.

Amaral-Phillips, D.M. 2016. Dairy feeding and management considerations during heat stress.http://articles.extension.org/pages/67811/dairy-feeding and management considerations during-heat-stress.

Armstrong, D.V. 1994. Heat stress interactions with shade and cooling. *Journal of Dairy Science* **77**: 2044 2050.

Bernabucci, U., Lacetera, N.L, Banmgard, H., Rhoads, R.P., Ronchi, B. and Nardone, A. 2010. Metabolic and hormonal acclimation to heat stress in domesticated ruminants. *Animal* **4**: 1167-1183.

Bernabucci, U.S, Biffani, L., Buggiotti, A., Vitali, N.L. and Nardone, A. 2014. The effects of heat stress in Italian Holstein dairy cattle. *Journal of Dairy Science* **97**: 471–486. doi:10.3168/jds.2013-6611.

Bianca, W. 1965. Relative importance of dry- and wet-bulb temperatures in causing heat stress in cattle. *Nature* **195**: 251–252.

Biffani, S.U, Bernabucci, A., Vitali, N.L and Nardone, A. 2016. Short communication: Effect of heat stress on non-return rate of Italian Holstein cows. *Journal of Dairy Science* **99**: 5837–5843. doi:10.3168/jds.2015-10491.

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

Bohmanova, J., Misztal. I., Tsuruta, S., Norman, H.D and Lawlor, T.J. 2005. National genetic evaluation of milk yield for heat tolerance of United States Holsteins. *Interbull Bull* **33**:160–162.

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

Bradford, H.L., Fragomeni, B.O., Bertrand, J.K., Lourenco, D.A.L. and Misztal, I. 2016. Genetic evaluations for growth heat tolerance in Angus cattle. *Journal of Animal Science* **94**: 4143–4150. doi:10.2527/jas2016-0707.

Brügemann, K., E. Gernand, U. U. von Borstel, and S. König. 2011. Genetic analyses of protein yield in dairy cows applying random regression models with time-dependent and temperature × humidity-dependent covariates. J. Dairy Sci. 94:4129–4139. doi:10.3168/jds.2010-4063.

Carabaño, M.J, Bachagha, K., Ramón, M., and Díaz, C. 2014. Modeling heat stress effect on Holstein cows under hot and dry conditions: selection tools. *Journal of Dairy Science* **97**: 7889–7904. doi:10.3168/jds.2014-8023

Carabaño, MJ.., Ramón, M., Díaz, C., Molina, A., Pérez-Guzmán, M.D. and Serradilla, J.M. 2017. Breeding for resilience to heat stress effects in dairy ruminants. A comprehensive review. *Journal of Animal Science* **95**: 1813–1826.

Chandra, V., Sejian, V. and Sharma, G.T. 2015. Strategies to Improve Livestock Reproduction under the Changing Climate Scenario. In: Climate Change Impact on Livestock: Adaptation and Mitigation, Prasad .Eds. *Springer Publisher*, New Delhi, India, pp: 425-440.

Charoensook, R., Gatphayak, K., Sharifi, A.R., Chaisongkram, C., Brenig, B., Knorr, C. 2012. Polymorphisms in the bovine HSP90AB1 gene are associated with heat tolerance in Thai indigenous cattle. Tropical Animal Health and Production **44**: 921-928.

Chen Siyu, Jian Wang, Dandan Peng, Gan Li, Jian Chen & Xianhong Gu. 2018. Exposure to heat-stress environment affects the physiology, circulation levels of cytokines, and microbiome in dairy cows**.** Scientific Reports, **8**: 14606.

Collier, R.J., Collier, J.L., Rhoads, R.P. and Baumgard, L.H. 2008. Genes involved in the bovine heat stress response. *Journal of Dairy Science* **91:**445–454.

Das, R., Sailo, L., Verma, N., Bharti, P., Saikia, J.I. and Kumar, R. 2016. Impact of heat stress on health and performance of dairy animals: A review. *Veterinary World* 9: 260-268.

Deb, R., Sajjanar, B., Singh, U., Kumar, S., Singh, R., Sengar, G., Sharma, A. 2013. Effect of heat stress on the expression profile of Hsp90 among Sahiwal .Bos indicus. and Frieswal .Bos indicus x Bos taurus. breed of cattle: a comparative study. *Genetics* **536**: 435-440.

Dekkers, J.C.M. and Hospital, F. 2002. The use of molecular genetics in improvement of agricultural populations. *Nature Review Genetics* **3**: 22–32.

Dekkers, J.C.M. 2004. Commercial application of marker- and gene-assisted selection in livestock strategies and lessons. *Journal of Animal Sciences* **82**: 313–328.

Dikmen, S., Alava, E., Pontes, E., Fear, J.M., Dikmen, B.Y., Olson, T.A. and Hansen, P.J. 2008. Differences in thermoregulatory ability between slick-haired and wild-type lactating Holstein cows in response to acute heat stress. *Journal of Dairy Science* 91: 3395-3402.

Dikmen, S., Cole, J.B., Null, D.J. and Hansen, P.J. 2012. Heritability of rectal temperature and genetic correlations with production and reproduction traits in dairy cattle. *Journal of Dairy Science* **95**: 3401–3405. doi:10.3168/ jds.2011-4306.

Dikmen, S., Khan, F.A., Huson, H.J., Sonstegard, T.S., Moss, J.I., Dahl, G.E. and Hansen, P.J. 2014. The SLICK hair locus derived from senepol cattle confers thermo-tolerance to intensively managed lactating Holstein cows. *Journal of Dairy Science* **97**: 5508–5520. doi:10.3168/jds.2014-8087.

Gaughan, J.B., Mader, T.L. and Gebremedhim, K.G. 2012. Rethinking heat index tools for livestock. *In: Collier, R. J., and J. L. Collier. Environmental physiology of livestock*. Chichester, West Sussex, UK: Wiley-Blackwell. doi:10.1002/9781119949091.

Gray, K.A, Smith, T., Maltecca, C., Overton, P., Parish, J.A. and Cassady, J.P. 2011. Differences in hair coat shedding, and effects on calf weaning weight and BCS among Angus dams. *Livestock Science* **140**: 68–71. doi:10.1016/j. livsci.2011.02.009.

Garner, J.B., Douglas, M., Williams, R. S. O, Wales, W. J., Marett L. C., Nguyen, T. T. T., Reich, C. M. & Hayes, B. J. 2016. Genomic selection improves heat tolerance in dairy cattle. Nature Scientific Reports 6:1-8.

Hahn, L.G. 1999. Dynamic Response of Cattle to Thermal Heat Loads. *Journal of Animal Science*, Vol. 51, E. Suppl. 1, January 1999., pp. 10-20, ISSN 0021-8112.

Henderson, C.R. 1984. Applications of linear models in animal breeding. University of Guelph, Guelp, Canada.

Hoffmann, A.A, Sorensen, J.G. and Loeschcke, V. 2003. Adaptation to Drosophila to temperature extremes: bringing together quantitative and molecular approaches. *Journal of Thermal Biology* **28:** 175 -216.

Igono, M. O., and H. D. Johnson. 1990. Physiological stress index of lactating dairy cows based on diurnal pattern of rectal temperature. J. Interdiscip. Cycle Res. 21:303 320.

Kabuga, J.D. 1992. The influence of thermal conditions on rectal temperature, respiration rate and pulse rate of lactating Holstein-Friesian cows in the humid tropics. International Journal of Biometeorology volume 36, pages 146–150.

Lee, D.H.K. 1953. Manual of field studies on the heat tolerance of domestic animals. Manual of field studies on the heat tolerance of domestic animals.

Lewin, B. 1994. Genes V. Oxford University Press.

Li, Q., Han, J., Du, F., Ju, Z., Huang, J., Wang, J., Li, R., Wang, C., Zhong, J. 2011. Novel SNPs in HSP70A1A gene and the association of polymorphisms with thermo tolerance traits and tissue specific expression in Chinese Holstein cattle. *Molecular Biology of Reproduction*. **38**(4). :2657–2663. doi: 10.1007/s11033-010-0407-5.

Macciotta, N.P.P., Biffani, S., Bernabucci, U., Lacetera, N., Vitali, A., Ajmone-Marsan, P. and Nardone, A. 2017. Derivation and genome-wide association study of a principal component-based measure of heat tolerance in dairy cattle. *Journal of Dairy Science* **100**: 4683–4697. doi:10.3168/jds.2016-12249.

María, J., Carabaño, Manuel Ramón, Alberto Menéndez-Buxadera, Antonio Molina, and Clara Díaz. 2019. Selecting for heat tolerance. doi: 10.1093/af/vfy033.

Niedz, R.P. 2007. The slick hair locus maps to chromosome 20 in Senepol-derived cattle. *Animal Genetics* **38:** 54-59.

Menéndez-Buxadera, A., Molina, A., Arrebola, F., Clemente, I. and Serradilla, J.M. 2012. Genetic variation of adaptation to heat stress in two Spanish dairy goat breeds. *Journal of Animal Breeding and Genetics* **129**: 306–315. doi:10.1111/j.1439-0388.2011.00984.x.

Min, L., Zhao, S., Tian, H., Zhou, X., Zhang, Y., Li, S., Yang, H., Zheng, N. and Wang, J. 2017. Metabolic responses and "omics" technologies for elucidating the effects of heat stress in dairy cows. *International Journal of Biometeorology 61*: 1149– 1158. doi:10.1007/s00484-016-1283-z.

Mosser, D.D., Caron, A.W., Bourget, L., Meriin, A.B., Sherman, M.Y., Morimoto, R.I., Massie, B. 2000. The chaperone function of hsp70 is required for protection against stress induced apoptosis. *Molecular Cell Biology* **20**: 7146–59.

Nguyen, T.T.T., Bowman, P.J., Haile-Mariamn, M., Nieuwhof, G.J., Hayes, B.J. and Pryce, J.E. 2017. Short communication: Implementation of a breeding value for heat tolerance in Australian dairy cattle. *Journal of Dairy Science* **100**: 7362–7367.

Nguyen, T.T.T., Bowman, P.J., Haile-Mariamn, M., Pryce, J.E. and Hayes, B.J. 2016. Genomic selection for tolerance to heat stress in Australian dairy cattle. *Journal of Dairy Science* **99**: 2849–2862. doi:10.3168/jds.2015-9685.

Olson, T.A., Lucena, C., Chase, C.C. and Hammond, A.C. 2003. Evidence of a major gene influencing hair length and heat tolerance in *Bos taurus* cattle. *Journal of Animal Science* **81**: 80 90.

Prathap, Pragna, Archana, P.R., Joy, Aleena, Veerasamy, Sejian, Govindan, Krishnan, Madiajagan Bagath, Manimaran, A., Beena, V., Kurien, E.K., Girish, Varma and Raghavendra, Bhatta. 2017. Heat Stress and Dairy Cow: Impact on Both Milk Yield and Composition. *International Journal of Dairy Science*. ISSN 1811-9743**.** Bangalore, India.

Pritchard, T., Coffey, M., Mrode, R., Wall, E. 2013. Genetic parameters for production, health, fertility and longevity traits in dairy cows. *Animal* **7**: 34-46.

Ramendra Das, Lalrengpuii Sailo, Nishant Verma, Pranay Bharti, Jnyanashree Saikia, Imtiwati, and Rakesh Kumar. 2016. Impact of heat stress on health and performance of dairy animals: A review. *Veterinary World* 9(3): 260–268.. doi: 10.14202/vetworld.2016.260-268.

Ramón, M, Díaz, C, Pérez-Guzman, M.D. and Carabaño, M.J. 2016. Effect of exposure to adverse climatic conditions on production in Manchega dairy sheep. *Journal of Dairy Science* **99**: 5764–5779. doi:10.3168/jds.2016-10909.

Ravagnolo, O. and Misztal, I. 2000. Genetic component of heat stress in dairy cattle, parameter estimation. *Journal of Dairy Science* **83**: 2126–2130. doi:10.3168/jds. S0022-0302.00.75095-8.

Sánchez, J. P., Misztal, I., Aguilar, I., Zumbach, B. and Rekaya, R. 2009. Genetic determination of the onset of heat stress on daily milk yield in US Holstein cattle. *Journal of Dairy Science* **92**: 4035–4045. doi:10.3168/jds.2008-1626.

Santana, Jr. M.L., Bignardi, A.B., Pereira, R.J., Menendez-Buxadera, A. and El Faro, L. 2016. Random regression models to account for the effect of genotype by environment interaction due to heat stress on the milk yield of Holstein cows under tropical conditions. Journal of Applied Genetics **57**: 119-127.

Santana, M.L. Jr, Pereira, R.J., Bignardi, A.B., Filho, A.E., Menéndez- Buxadera, A. and El Faro, L. 2015. Detrimental effect of selection for milk yield on genetic tolerance to heat stress in purebred zebu cattle: genetic parameters and trends. *Journal of Dairy Science* **98**: 9035–9043. doi:10.3168/jds.2015-9817.

Seath, D.M. 1947. Heritability of heat tolerance in dairy cattle. J. Dairy Sci. 30: 137–144.

Schüller, L.K., Burfeind O., and Heuwieser W. 2014. Impact of heat stress on conception rate of dairy cows in the moderate climate considering different temperature–humidity index thresholds, periods relative to breeding, and heat load indices. Theriogenology. 81 (8): 1050-1057.

Schwerin, M., Brockmann, G., Vanselow, J. and Seyfert, H.M. 1995. Perspectives of molecular genome analysis in livestock improvement. *Archive Tierz Dummerstorf* **38**: 21-31.

Silanikove, N. 2000. Effects of heat stress on the welfare of extensively managed domestic ruminants. *Livestock Production Science* **67**: 1-18.

Sorensen, J.G., Kristensen, T.N. and Loeschcke, V. 2003. The evolutionary and ecological role of heat shock proteins. *Ecology Letters* **6:** 1025-1037.

Stein, G.S., Stain, J.L., Van, Wijnen, A.J. and Lian, J.B. 1996. The maturation of a cell. *American Scientist* **84**: 28-37.

St-Pierre, N.R., Cobanov, B. and Schnitkey, G. 2003. Economic losses from heat stress by US livestock industries. *Journal of Dairy Science* **86**: E52-E77.

Van Goor, A, Ashwell, C. M., Persia, M.E., Rothschild, M.F., Schmidt, C.J. and Lamont, S.J. 2016. Quantitative trait loci identified for blood chemistry components of an advanced intercross line of chickens under heat stress. **BMC Genomics** 17: 287.

Wang, Z., Wang, G., Huang, J., Li, Q., Wang, C. and Zhong, J. 2011. Novel SNPs in the ATP1B2 gene and their associations with milk yield, milk composition and heat-resistance traits in Chinese Holstein cows. Molecular Biology Reproduction. **38** (3): 1749–1755.

West, J.W. 2003. Effects of heat-stress on production in dairy cattle. *Journal of Dairy Science* **86**: 2131 2144.

West, J., Mullinix, B. and Bernard, J. 2003. Effects of hot, humid weather on milk temperature, dry matter intake, and milk yield of lactating dairy cows. *Journal of Dairy Science* **86(**1), 232-242.

Yousef, M.K. 1985. Stress Physiology in Livestock. CRC Press, Boca Raton, FL, USA.