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Importance of heat shock protein 70 in livestock - at cellular level

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ABSTRACT

Heat stress is a condition when the environmental temperature is higher than the upper critical temperature of the animal's core body temperature. This results in an imbalance in body homeostasis of the animal. A large number of proteins are being constantly expressed in the animal's body during the time of heat stress. Among all those proteins, heat shock proteins (HSPs) are the major family of proteins that have shown a great potential to ameliorate the deleterious effects of heat stress. HSP70 is a ubiquitously expressed protein, which protects cell from heat stress by maintaining cellular machinery through proper folding of denatured proteins and preventing cellular apoptosis. Therefore, it is paramount to know the mechanism of cellular protection by prevention of apoptosis during heat stress. The present review highlights the regulatory role of HSP70 on cellular machinery during heat stress.

KEY WORDS: Cell, heat shock protein 70, heat stress, livestock

INTRODUCTION

Homeotherms (mammals and birds) have got the ability to maintain a constant body temperature irrespective of their surrounding temperature; still they are susceptible to various types of stress. Stress represents the reaction of the body to stimuli that disturbs the normal homeostasis often with detrimental effects [1]. The stress could be physical, physiological, nutritional, chemical, psychological and environmental. Under stressful conditions, physiological and behavioral responses vary in relation to the genetic makeup of the animal. Among the various types of stressor, high environmental temperature is a major concern in the tropical and arid areas that alters normal homeostasis of animals [2]. Heat stress occurs when animals are exposed to temperature beyond the upper critical level causing an increase in heat production in the animal body. Along with high ambient temperature, high humidity and low air movement further exacerbates the condition [3]. Thermal stress inhibits many complex responses which are essentials in the preservation of cell survival [4]. Warm blooded animals used to escape this harmful effect of heat stress by their heat adaptability mechanism. Heat adaptability is a complex phenomenon that depends on the integrity of various systems such as respiratory, circulatory, excretory, nervous, endocrine, enzymatic and acid-base buffer systems of the body. The coordination of all these systems to maintain the productive potential against heat stress is inconsistent that not only varies between species but also between breeds and even between individuals within the same breed. At cellular level, heat stress causes protein misfolding, which are corrected by induced expression of certain molecules, function like molecular chaperone, regarded as heat shock proteins (HSPs). Among various HSPs characterized, HSP70 is well correlated with the development of thermo tolerance in many cell types [5]. The main objective of this review is to provide the detail regulatory mechanism of HSP70 on cellular protection during heat stress.

CELLULAR RESPONSE TO HEAT STRESS

Cellular homeostasis is maintained by balancing net growth and death rate of cells [6]. Cells have got their own way to tackle the adverse conditions by up-regulating certain sets of genes and turning down others. One of the main cellular consequences of heat stress is protein damage leading to the aggregation of unfolded proteins. In order to offset this, cells raise the expression of chaperone proteins that help in the refolding of

misfolded proteins and assuage protein aggregation. The set of genes which are activated under unfavourable conditions encode for HSPs. By helping to stabilize partially unfolded proteins, HSPs aid in transporting proteins across membranes within the cell [7]. Cells can respond to thermal insult either by switching on survival pathways or commencement of cell death and ultimately removing damaged proteins.

HSP70 AS MOLECULAR CHAPERONES

HSPs act as molecular chaperones. These molecular chaperon protect the three dimensional structure of proteins of an organism once it has been exposed to an environmental insult [8]. Cells that have recovered from a mildly stressful episode express elevated levels of HSPs and can exhibit tolerance to potential stressors that would normally cause developmental abnormalities or death. The role of HSPs has been identified in most of the livestock species [9]. Among members of the HSP family, HSP70 (namely, HSP70-1 and HSP70-2) is the most abundant and temperature sensitive [10]. The 70 kDa HSP family (HSP70) has been categorized into constitutive and inducible forms [11], which contribute to stress tolerance by escalating the chaperone activity in the cytoplasm [12]. The inducible form of HSP70 (HSP70i) has been proposed as a forecaster for thermo tolerance at cellular level [13,14] and is well correlated with development of thermo tolerance in many cell types [5]. Heat stress induced HSP70 expression was observed in bovine lymphocytes [15-17] and in kidneys of goats [18]. During thermal stress in human lymphocytes, HSP70 expression is escalated and protects these cells from toxic effects [19]. Dangi *et al*. [20] reported the effect of seasonal variation on HSPs expression in caprine peripheral blood mononuclear cells (PBMCs) and found that expression of HSP70 was elevated during peak summer season as compared to peak winter in both tropical and temperate region goats. In addition to improving overall protein integrity, HSP70 directly inhibits cellular apoptosis [21]. This cellular response may be an important mechanism by which animals are able to protect cells from heat stress. HSP70 have been found to play a neuroprotective role in several models of neurodegeneration both *in vivo* and *in vitro* [22]. Zulkifli *et al*. [18] observed that the transportation under hot, humid tropical conditions significantly increased HSP70 densities in the renal cells of Boer does. Mishra *et al*., [17] found 200 fold increase in serum HSP70 levels in Murrah buffalo calves in heat stress conditions. Thermal exposure of Murrah buffalo heifers caused an induction of HSP70 but declined the lymphocyte proliferative response and interleukin-2, indicative of HSP70 as a marker for heat stress and reduced immune status of buffalo heifers [23]. Differences in HSP70 expression may be an indication of species' differences in thermo tolerance [24]. Higher expression of HSP70 in caprine PBMCs during heat stress, suggest a possible involvement of HSP70 in ameliorating the deleterious effect of thermal stress so as to maintain cellular integrity and homeostasis in goats [20]. Currie and Tufts [25] reported that rainbow trout (*Oncorhynchus mykiss*) red blood cells synthesize HSP70 in response to temperature stress.

CONCLUSION

Rising environmental temperature as a result of global warming is posing deleterious impact on production and productivity of animals. Due to thermal stress a large proportion of energy is channelized to maintain normal body temperature and offset the effect of heat stress. Major amount of body energy is utilized to maintain thermal equilibrium by heat acclimatization mechanism. Heat acclimatization mechanism diverts most of the heat energy produced during work by increased heat dissipation through cutaneous vasodilation. Therefore, heat acclimatization mechanism maintains the core body temperature so that the animals continue to perform increased work in elevated temperature. The main role of HSP70 is to prevent the deleterious effects of heat stress by inhibiting cellular apoptosis. These are the endogenous mechanisms by which animals adapt to the elevated environmental temperature. There are also various external approaches to maintaining animal core body temperature during heat stress by providing proper shading materials, water sprinkler and use of water coolers. HSPs are instrumental in conferring thermo tolerance in livestock at cellular level but other physical measures like providing shade, sprinklers; coolers at animal shades must be opted to reduce the extent of thermal stress. A thorough understanding about the mechanism of various HSPs at cellular level during heat stress not only helpful to mitigate the harmful effects of heat stress but also to increase the production and productivity of animals, which will improve the socioeconomic status of the farmers as well as the country.

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