

Review Article

HEAT SHOCK PROTEIN USES IN VACCINE DEVELOPMENT FOR INFECTIOUS DISEASES AND CANCER

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ABSTRACT

Objectives: Heat Shock protein or Heat stress protein (Hsp) are produced by all organisms to overcome heat stress. Henceforth, they are critical controllers of cell multiplication, separation and unequivocally embroiled in the sub-atomic coordination of malignant growth improvement and movement the same number of their customers is settled oncoproteins in numerous tumor types.

Methods: Curiously, tumor cells are more HSP chaperonage-subordinate than ordinary cells for multiplication and endurance on the grounds that the oncoproteins in malignant growth cells are frequently misfolded and require enlarged chaperonage movement for rectification. It also enhances survival rate of organisms. It also acts as immunogen in the host. So it is useful to vaccine development.

Results: The production cost of Hsp is low, production method and isolation technique is also easy.

Conclusion: If it is combined with DNA vaccine, it will produce long-term immunity.

Keywords: Heat shock protein, Heat stress protein, Vaccine.

INTRODUCTION

All the living organisms respond at the cellular level to unfavourable conditions. During stress, small number of specific genes is expressed. The essential capacity of the resistant reaction is to recognize particles, generally proteins, that are translated as either segments of self or nonself atoms likely got from attacking living beings. Through the systems of focal and fringe resistance, the safe reaction is dissuaded from assaulting cells perceived as self [1, 2]. During heat shock, the genes produced proteins which are commonly referred to as heat shock proteins or heat stress proteins. When cells are exposed to physiological and environmental insults such as hyperthermia, ischemia, anoxia, toxins or ultra violet (UV) light, viral particles, surgical/emotional/mechanical or other types of stress, one natural defense response is to dramatically augment the synthesis of a small group of proteins that are commonly known as "heat-shock" proteins (HSPs). Elevated expression of these stress proteins allows the cells to withstand otherwise lethal condition(s). HSPs are evolutionarily conserved and ubiquitously expressed in all organisms and in different subcellular compartments [3, 4]. These are present very lesser amount in normal condition, But during stress conditions it increases higher concentrations [5]. During heat shock, the induction of the stress response can be mediated by many adverse environmental factors. The mechanism by which these may stimulate the stress response appears to converge at the level of transcription and as such it is the activity of heat shock transcription factors which appears to regulate the expression of stress proteins [6]. In addition to maintaining cell homeostasis under physiological and stress conditions, some heat shock proteins (HSPs) are potent inducers of immunity and have been harnessed as vaccine adjuvants targeted to cancers and infections. HSPs are a group of ubiquitous intracellular molecules that function as molecular chaperones in numerous processes, such as protein folding and transport, and are induced under stress conditions, such as fever and radiation [19].

THERMOTOLENCE

Thermotolerance relates to the ability of a cell to survive an extreme insult following the exposure to mild stress. When organisms are exposed to a sufficiently severe heat shock or stress, the majority of organisms are die. If however, prior to this lethal

heat shock they undergo a mild heat treatment, a considerable proportion of them survive. A mild heat shock will protect against a potentially lethal oxidative stress 24 hours later. This tolerance is dependent upon the successful production of stress proteins in response to earlier stress. [7, 8]. The presence of abnormal proteins can trigger the activation of the stress response providing an indication of a possible role for these proteins in binding to aberrant polypeptide structures. In the late 1980s through genetic analysis and cell biological research it became clear that the major stress proteins were acting as molecular chaperones in a variety of cellular systems [9].

MATERIALS AND METHODS

MOLECULAR CHAPERONES

The cytoplasm of a cell is a complex soup of proteinaceous material and even the simplest proteins contain many structural elements. Although the secondary structure of a protein is dictated by the amino acid sequence the way in which secondary structural (figure 1) elements combine to form the tertiary and quaternary structures which also depends upon the correct alignment of these secondary elements and their subsequent hydrogen bonding. Strong structural motifs, such as alpha helices, contain many hydrophobic residues which may interact with incorrect domains during protein folding, this would lead to protein aggregation and a dysfunctional product [10]. The term molecular chaperone was first used by Ron Lasky and his co-workers to describe the role of nucleolus in mediating nucleosome assembly. Although the concept is essentially that of catalysts of protein structure [11]. The molecular chaperones are defined as a functional class of unrelated families of proteins that mediate the correct non-covalent assembly of other polypeptide containing structures, but are not the components of these assembled structures, when the latter carrying out their normal biological functions. The functions of the molecular chaperones are universal cellular functions. Defined as the prevention of incorrect interactions between transiently exposed interactive surfaces by the binding of molecular chaperones to those surfaces. The molecular chaperones help to prevent these aberrant interactions by binding to hydrophobic regions. Additionally, most proteins need to be in a relatively unfolded state in order for them to pass through cellular membranes, so molecular chaperones

are involved in keeping polypeptides in trans location and transport competent state and in their subsequent post translocation folding [12].

IMMUNOGEN

Heat shock proteins are useful in immunogenic adjuvant which is helpful to boost up the efficacy of vaccine. It acted as good component of vaccine. In our lab, one experiment was conducted in heat shock protein. In this study, bacterial pathogen *Staphylococcus aureus* was collected from local hospital lab. The pathogen was introduced in broth, after 24 hours it was centrifuged and pellet was

collected. The pellet was washed with physiological saline, and then it was treated with two sets of temperature 50 c and 55 c respectively. This was treated with different time treatment. (0, 10, 20, 30&40 minutes)The Hsp was isolated with acetone precipitated method. These are mixed with saline solution and it was injected to albino rats by intramuscular injection. The blood samples were collected after two weeks and taken for analysis. From this attempt it was determined the optimum dosage 55 c,10 minutes produced heat shock protein induces a maximum immune response in the host. Hence it is recommended that Hsp can be used as immunogenic part or adjuvant for the development of *S.aureus* vaccine [13].

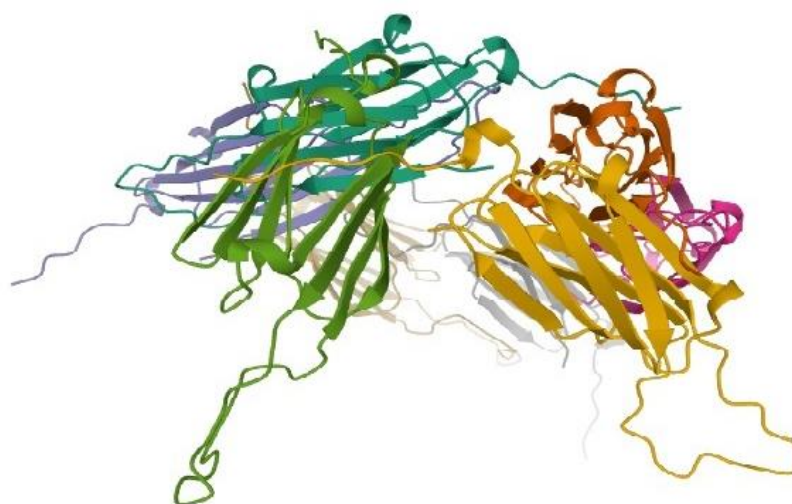


Fig. 1: Heat protein 1SHS (Source PDP).

RESULTS AND DISCUSSION

The optimum range of Heat Shock Protein (Hsp) induces higher level of immunity. These will be used as vaccine immunogen or use as vaccine adjuvant for induces vaccine immunity. Mortality rate of cancer is becoming unacceptably high and is, therefore, a worldwide anxiety. [14]. are not the part of pathogenic bacteria. So it cannot produce diseases. If use these protein in vaccine preparation, it induces immunity only. These proteins preparations and collection method are easy. For specific disease, it is use as immunogen and other infectious diseases; it will be use as adjuvants. So any how it is part of vaccine development. It has many advantages for use as part of vaccine. If it is combined with Plasmid DNA, it will give long term immunity. So it is highly suitable for vaccine preparation [15-17]. Heat shock proteins protecting against stress these molecules are also folding and assembling of proteins within the cells. Hsp is combinations with peptides, protected mice from developing cancer in lab experiments. This Hsp protein and associated peptide complexes also isolated from a patient's tumour. Hsp treatment of several human cancers including liver, Skin, colon, long lymphoma and prostate [18] The Heat shock proteins cannot produce diseases. So it is safer one for vaccine preparations. These are proteins; it induces immunity at very short duration. These protein production and isolation methods are easy. For production, it requires minimum facilities. It also requires minimum facilities. It also requires slow production cost. It act as immunogen for specific infectious diseases and it is also antigenic protein. So it is useful to prepare peptide vaccine for bacterial infectious diseases. It is also useful to prepare vaccine for more than one infectious disease. It is also suitable for pain free immunization methods.

CONCLUSION

Heat shock protein is new sources for simple vaccine development for bacterial infectious diseases. It acts as adjuvant for any bacterial vaccine. For specific infections, it acts as immunogen and it also use in new vaccine preparation. Because it cannot produce diseases, it can induce only immunity. In combined with DNA vaccine it produces long term immunity.

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REFERENCE

1. Nikolich-Zugich, J., M.K. Slifka, and I. Messaoudi, *The many important facets of T-cell repertoire diversity*. Nature Reviews Immunology, 2004. 4(2): p. 123-132.
2. Walker, L.S. and A.K. Abbas, *The enemy within: keeping self-reactive T cells at bay in the periphery*. Nature Reviews Immunology, 2002. 2(1): p. 11-19.
3. Jäättelä, M., *Heat shock proteins as cellular lifeguards*. Annals of medicine, 1999. 31(4): p. 261-271.
4. Jego, G., et al., *Targeting heat shock proteins in cancer*. Cancer letters, 2013. 332(2): p. 275-285.
5. Beckmann, R.P., L. Mizzen, and W.J. Welch, *Interaction of Hsp 70 with newly synthesized proteins: implications for protein folding and assembly*. Science, 1990. 248(4957): p. 850-854.
6. Hutter, M.M., et al., *Heat-shock protein induction in rat hearts. A direct correlation between the amount of heat-shock protein induced and the degree of myocardial protection*. Circulation, 1994. 89(1): p. 355-360.
7. Enjalbert, B., A. Nantel, and M. Whiteway, *Stress-induced gene expression in Candida albicans: absence of a general stress response*. Molecular biology of the cell, 2003. 14(4): p. 1460-1467.
8. Estruch, F., *Stress-controlled transcription factors, stress-induced genes and stress tolerance in budding yeast*. FEMS microbiology reviews, 2000. 24(4): p. 469-486.
9. Angelidis, C.E., I. Lazaridis, and G.N. Pagoulatos, *Constitutive expression of heat-shock protein 70 in mammalian cells confers*

- thermoresistance*. European journal of biochemistry, 1991. 199(1): p. 35-39.
10. Barazone, M., *Paving fabric interlayer membranes and installation procedures over the past 20 years*. Geotechnical Fabrics Report, 1990. 10(4).
 11. Georgopoulos, C. and W. Welch, *Role of the major heat shock proteins as molecular chaperones*. Annual review of cell biology, 1993. 9(1): p. 601-634.
 12. Hansen, L.K., J. Houchins, and J.J. O'Leary, *Differential regulation of HSC70, HSP70, HSP90 α , and HSP90 β mRNA expression by mitogen activation and heat shock in human lymphocytes*. Experimental cell research, 1991. 192(2): p. 587-596.
 13. Muruganandam, M., *Engineered plasmid DNA vaccine for Staphylococcus aureus*. Int J Biol Technol, 2011. 2(1): p. 7-10.
 14. Tamizhazhagan, V., et al., *Social and Economic Burden of Cancer on 2020-Minireview*. J Biol Med Sci, 2017. 1(103): p. 2.
 15. Petrovsky, N. and J.C. Aguilar, *Vaccine adjuvants: current state and future trends*. Immunology and cell biology, 2004. 82(5): p. 488-496.
 16. Adams, A. and K.D. Thompson, *Biotechnology offers revolution to fish health management*. Trends in biotechnology, 2006. 24(5): p. 201-205.
 17. Cleland, J.L., *Single-administration vaccines: controlled-release technology to mimic repeated immunizations*. Trends in biotechnology, 1999. 17(1): p. 25-29.
 18. Olle, D.A., *Treating Cancer with Immunotherapy and Targeted Therapy*. 2019: Stylus Publishing, LLC.
 19. Segal BH, Wang XY, Dennis CG, et al. Heat shock proteins as vaccine adjuvants in infections and cancer. Drug Discovery Today. 2006 Jun;11(11-12):534-540. DOI: 10.1016/j.drudis.2006.04.016.