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RESEARCH ARTICLE

IMPLICATION OF HEAT SHOCK PROTEINS IN PERIODONTAL DISEASE

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ABSTRACT

Heat shock proteins are found in virtually all living organisms, from bacteria to humans. Theystabilize proteins and are involved in the folding of denatured proteins.During the infection, HSP from several bacterial species are recognized by host as immunodominant antigens. Periodontopathic bacteria have sequence homology with human HSP 60 at amino acid level, which raises the possibility of cross reactivity. The present review gives an insight into the role of HSPs in the etiopathogenesis of periodontal disease.

INTRODUCTION

Heat shock proteins(HSP) are a class of functionally related proteins whose expression is increased when cells are exposed to elevated temperatures or other stress.This increase in expression is transcriptionally regulated.The dramatic upregulation of the heat shock proteins is a key part of the heat shock response and is induced primarily by heat shock factor(HSF).HSPs are found in virtually all living organisms,from bacteria to humans.[1]

Heat-shock proteins are named according to their molecular weight.For example, Hsp60,Hsp70 and Hsp90 (the most widely-studied HSPs) refer to families of heat shock proteins on the order 60,70 and 90 kilodaltons in size respectively.The small 8 kilodaltonprotein ubiquitin, which marks proteins for degradation,also has features of a heat shock protein.

Heat shock proteins are present in cells under normal conditions,but are expressed at high levels when exposed to a sudden temperature jump or other stress.Heat shock proteins stabilize proteins and are involved in the folding of denatured proteins.High temperature and other stresses such as altered pH and oxygen deprivation,make it more difficult for proteins to form their proper structures and cause some already structured proteins to unfold.Left uncorrected,mis-folded proteins form aggregated that may eventually kill the cell.Most heat shock proteins are molecular chaperones.Chaperones aid in the transport of proteins throughout the cell's various compartments.[2]

Under normal conditions,heat shock proteins are required for cellular metabolism and help newly synthesized poly peptides fold,thus preventing premature interactions with other proteins.

In 1962, Ritossa reported that heat and the metabolic inhibitor dinitrophenol induced a characteristic pattern of puffing in the chromosomes of Drosophila. This discovery eventuallyled to the identification of the heat-shock protein (HSP) or stress proteins whose expressionthese puffs represented.Increased synthesis of selected proteins in Drosophila cells following stresses such as heat shock was first reported in 1974.[3]

Classification of heat shock proteins: [4]

The principal heat-shock proteins that have chaperone activity belong to five conserved classes; HSP33,HSP60,HSP70,HSP90,HSP100 and the small heat-shock proteins(sHSPs).

Extracellular stress proteins: [5]

Osteonectin/ (Secreted Protein Acidic and Rich in Cysteine) SPARC

Osteonectin/SPARC is a 32 kDa phosphorylated glycoprotein protein originally purified from bone tissues, has been identified in several tissues, including placenta, platelets and fibroblasts. Analyses of protein structures have indicated that osteonectin and SPARC are identical.

Thrombospondin

Thrombospondin (TSP) is a trimeric extracellular matrix protein that binds to cells through membrane-associated heparin sulfate proteoglycans.

Other Proteins

It is interesting that mRNA of two metalloproteinases, collagenase and stromelysin which are produced in large quantities in rheumatoid arthritis, diabetes, periodontal disease and connective tissue undergoing remodeling are expressed by heat shock.

Role of HSP in periodontal diseases

HSP are perhaps, are investigated extensively as a self antigens in periodontal diseases. On exposure to environmental factors, these proteins participate in various processes like folding and translocation of polypeptides across the membranes. These HSP can also be referred as molecular chaperones.

During the infection, HSP from several bacterial species are recognized by host as immunodominant antigens. Periodontopathic bacteria have sequence homology with human HSP 60 at amino acid level. These proteins are found in the tissues samples of periodontitis lesions.

HSP 60 is considered as very immunogenic and the autoimmune response to it could be touted as the initiator of inflammatory diseases.It is hypothesized that the periodontopathic bacteria stimulate the cells of periodontium to secrete amount of HSP 60 expression which inturn leads to exaggerated secretion of proinflammatory cytokines by macrophages. (Pleguezuelos et al)[6]

It was reported initially that the expression of HSP 60 was higher in gingivitis and periodontitis tissue

extracts compared to healthy tissue. (Lundqvist et al [7], Petit et al[8], Ueki et al[9])

Yamazaki et al[10]and Choi et al[11] demonstrated HSP specific T cell might be involved in the immunopathogenesis of periodontal diseases.

Recent paper by Nethravathy et al[12]reported increased levels of Circulatory HSP 60 in periodontal disease compared to health individuals.

Molecular mimicry:Role of HSP 60 in periodontal diseases-cardiovascular disease link[13]

The concept of molecular mimicry was introduced by Raymond Damian in 1964. He suggested that antigenic determinants of microorganisms may share homology with antigenic determinants of their hosts. It was hypothesized that molecular mimicry may induce cross reactive immune response with host antigens, resulting in an autoimmune disease like mechanism.

This mechanism was touted as fundamental for atherogenesis. Endothelial cells under stressful conditions express heat shock proteins. In addition, periodontopathic bacteria ieP.gingivalis express heat shock proteins like proteins such as GroEL. It was proposed that structural homology exists between HSP 60 and GroEL of P.gingivalis, the anti P.gingivalis immune response cross-reacts with human HSP 60 expressed on endothelial cells, resulting in endothelial dysfunction and atherosclerosis.

Conclusion

Heat shock proteins and their role in etiopathogenesis of periodontal disease would aid in diagnosing and treating the disease. HSP could be considered as a potential candidate antigen for periodontal vaccine.

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