Abstract: Heat shock/stress proteins (HSPs) are crucial for maintenance of cellular homeostasis during normal cell growth and for survival during and after various cellular stresses. The HSP70 family functions as molecular chaperones and reduces stress-induced denaturation and aggregation of intracellular proteins. In addition to the chaperoning activities, HSP70 has been suggested to exert its protective action by protecting mitochondria and by interfering with the stress-induced apoptotic program. The biochemical and functional properties of HSPs observed in cultured cells may be relevant to organs and tissues in whole animals. The activation of the hypothalamic-pituitary-adrenal axis and the sympathetic nerve system elicits the stress response in selected peripheral tissues; the HSP70 expression in the vasculature and stomach increases resistance against hemodynamic stress and stress-induced mucosal damage, respectively. Gastric mucosa pretreated with mild irritants acquires a tolerance against subsequent mucosal-damaging insults. This phenomenon is known as “adaptive cytoprotection”. Transient ischemia also induces ischemic tolerance in the brain and heart, which is called “ischemic preconditioning”. The heat shock response is believed to contribute to the acquisition of the tolerance. The therapeutic applications of chaperone inducers that induce HSPs without any toxic effect are also introduced. J. Med. Invest. 44: 137-147, 1998

Key Words: heat shock/stress proteins, physiologic stress, stress ulcer, ischemic tolerance, chaperone inducers
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The diagram shows the relationship between stress and the transition of HSF1 (inactive) to HSP gene expression. The stress signal triggers a cascade of events that leads to the activation of HSF1, which then binds to the HSE region of the HSP gene promoter, inducing its expression. This process is crucial in cellular responses to stress, allowing cells to withstand and recover from stressful conditions.

The diagram illustrates the movement of stress from the cytosol to the nucleus, where HSF1 is activated and binds to the HSE region of the HSP gene promoter. This binding leads to the transcription of the HSP gene, which is essential for cellular survival under stressful conditions.

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Restraint and water-immersion stress

Hypothalamus (CRF)

Pituitary gland (ACTH)

Brain stem

Sympathetic nerve

Adrenal gland

Vagus nerve

Glucocorticoids

Catecholamines

Stomach

A Hypothalamus

HSP70 mRNA/GAPDH mRNA

Control

Low protein

B Adrenal gland

C Stomach

Vagotomy

HSP70 mRNA/GAPDH mRNA

Control

Low protein

Adrenalectomy

A Hypothalamus

B Adrenal gland

C Stomach

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Chaperone inducers

1. Ischemia/reperfusion injury
2. Trauma
3. Inflammation
4. Infection
5. Stress ulcer