Heat Shock Response in Drosophila

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INTRODUCTION

Temperature is a very important environmental factor with profound effect on biological activities. Although the range over which temperature varies in different habitats and at different seasons is very wide, a given species is normally exposed to a rather narrow range of temperatures variations and usually suffers if exposed to temperatures lower or higher than this "physiological range". A living organism displays a wide variety of physiological, behavioral and other adaptions to protect itself from adverse effects of environmental temperatures beyond its physiological range. However, in addition to these organism-level adaptive responses, individual cells also cope up with sudden increase in their surrounding temperature by altering their transcriptional, translational and other activities in a characteristic fashion. All these changes in cellular activity in response to the sudden increase in surrounding temperatures beyond the physiological range are collectively termed the "heat shock response". In recent years, the topic of heat shock response has been reviewed many times and has also been the subject matter of several symposia. Some general reviews of this topic may be found in Lindquist (1986), Bienes & Pochon (1987), Lindquist and Craig (1988), Burdon (1988), Pochon (1989), Bond and Schatz (1990), Schatz (1990), Monticino et al (1990), Nagao et al (1995). This article covers primarily the basic aspects of heat shock response in Drosophila.

F. Ritossa for the first time used polytene chromosomes of Drosophila larvae to examine the cellular response to heat shock in the form of newly induced puff (Ritossa, 1962, 1964). Further interest in the heat shock response was stimulated when it was shown that the induction of new puffs by heat shock in salivary gland polytene chromosomes was associated with synthesis of a new set of polypeptides, the heat shock polypeptides. Following these seminal studies on the heat shock response using Drosophila cells, many researchers began to examine the cellular response to heat shock in a wide variety of organisms. Techniques available in early 70's did not permit a direct study of heat shock induced gene activity in organisms that lacked polytene chromosomes, but the discovery of induced synthesis of heat shock polypeptides in Drosophila stimulated search for a similar response in other organisms. Since then it has been a rather simple approach in all kinds of living systems. These studies not only revealed that all organisms show a comparable heat shock response, but that a variety of other cellular stress conditions also elicit a similar response.

During the past two decades, the heat shock response has been studied extensively in pro and eukaryotes. Initially an important consideration for these studies was that the conditional switching on of the heat shock genes provided a simple but elegant model system for wide standing the mechanism of gene expression and regulation at transcriptional and translational levels. More recent years, the emphasis has shifted to biological significance of the heat shock response and the role played by heat shock polypeptides in normal life under conditions of cellular stress.

THE HEAT SHOCK RESPONSE IN DROSOPHILA

Heat shock induces new puffs and new species of RNA

The special structure of polytene chromosomes: salivary glands of late 3rd instar larva of Drosophila termite a direct visualization of any alteration in gene.
Fig. 1. Heat shock induced puff in polytene chromosomes of Drosophila melanogaster. Polytene chromosomes from a non-heat shocked salivary gland were grown as a whole tissue after heat shock; see legend p. 19b. For heat shock, salivary glands of one third instar larvae (grown at 24°C) were kept at physiological saline solution at 37°C for 30 min prior to acetocarmine stained squash preparation. The characteristic banding pattern (alternate dark and light stained region) of these giant chromosomes in polytene nthoica permits easy identification of not only individual chromosomes and their arms (left and right arm in the case of a metacentric or sub-metacentric chromosome) but also of specific chromosome regions. Each such stained arm is given a number following a standard numbering system: the different heat shock puffs are designated after the number of the band that puff(s) out in response to heat shock. X = X chromosome; 2L and 2R = left and right arms, respectively, of chromosome 2; 3L and 3R = left and right arms, respectively, of chromosome 3; and 4 = the major heat shock induced puff on 3L and 3R are also marked: these regions appear not-puffed in a control but no puff is in 4 (heat checked).

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activity (see the article "Polytene Chromosome Puffing and Gene Expression" in this issue) since the active regions are visible as distinct puffs under light microscopy (see Fig. 1). Puffs are locally decondensed regions with an enlarged diameter and lighter staining. It was shown (see Beerlinnann 1972) that a local decondensation of the parallelly aligned multitudes of sister chromatid fibrils (staining due to repeated endoreduplication) of a polytene chromosome was necessary for active transcription at the puff site. Thus the appearance of a puff is indicative of transcriptional activity at the site.

Taking advantage of the phenomenon of puffing in polytene chromosomes of Drosophila larvae, Reithoff (1965, 1966) examined effect of brief exposure of larval salivary glands to 37°C or to 2,4-dinitrophenol or NaBtaurate. It was found that new transcriptionally active puffs were seen at certain specific regions of the polytene chromosomes in the treated glands while in untreated control glands no puffs were even seen at those sites.

It was remarkable that all the three treatments led to expression of previously existing puffs and induction of the same set of new puffs, the heat shock puffs. Studies with polytene chromosomes of D.melanogaster identified the following 9 loci (named after designation of the polytene band that is involved in puffing) as the heat shock puff sites: 33B on 2L, (left arm of chromosome 2), 63BC, 64EP, 67B, and 70A on 3L (left arm of chromosome 3), 87A, 87C, 93D and 55D on 3R (right arm of chromosome 3). Of these, the heat shock induced puffs at 63BC, 67B, 87A, 87C and 93D are relatively large and are considered as the major heat shock puff sites (Asbdurser, 1970; Asbdurser and Bonner, 1979; Munketjer and Lasko, 1979; see Fig. 1). In a very elegant study, Spindling et al. (1977) fractionated the H-serine labeled poly A- and poly A+ RNA from heat shocked salivary glands of D. melanogaster larvae by gel electrophoresis and hybridized individual fractions to polytene chromosomes in situ. This study confirmed that the different heat shock puffs arise distinct mRNAs.

Heat shock induces synthesis of new polyseptate proteins To study the effect of heat shock on protein synthesis in cells, Tissières et al. (1974) and Lewis et al. (1975)
labelled the newly synthesized proteins in control and heat shocked cells from different tissues of *Drosophila* larvae, pupae and adults with radiolabeled amino acids. Polypeptides from such control and heat shocked cells were fractionated by sodium-decyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE). The newly synthesized polypeptides were then identified by autodigestion of the gels (the newly synthesized polypeptides only had incorporated radio labelled amino acids these could be detected on X-ray film placed in close contact with the gel). A comparison of the labelled polypeptide bands in samples from control and heat shocked cells of different tissues revealed that while the types of polypeptides-synthesized in different cell types under control (non-heat shock) condition varied in a tissue-specific manner, the heat shocked cells of all tissues synthesized the same set of 7 different polypeptides that were generally not synthesized in control cells. The apparent molecular weights (in kilodaltons, kD) of these heat shock induced polypeptides were 82KD, 70KD, 69KD, 27KD, 26KD, 23KD and 22KD (see Fig. 2). These were termed the heat shock polypeptides or hsp.

**Heat shock induced polypeptide transcripts and polypeptides are correlated**

Subsequent application of other molecular, genetic and recombinant DNA techniques permitted a correlation of the different hsp with specific cDNA probes and their transcripts. Location of the different heat shock genes on polytene chromosomes and the products made by them in *D. melanogaster* are given in Table 1.

<table>
<thead>
<tr>
<th>Polyene Chromosomes</th>
<th>Gene</th>
<th>Product</th>
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<tr>
<td>Puff Site</td>
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<tr>
<td>63H</td>
<td>pse 83</td>
<td>83KD hsp</td>
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<tr>
<td>66F</td>
<td>Poly(A)</td>
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<td>64F</td>
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<tr>
<td>67B</td>
<td>hsp 27</td>
<td>27KD hsp</td>
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<td></td>
<td>gene 1</td>
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<td></td>
<td>gene 3</td>
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<tr>
<td>70A</td>
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<td>hsp 70</td>
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<td></td>
<td>alpha-beta</td>
<td>RNA</td>
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<td></td>
<td>repressor</td>
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<td>63D</td>
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<td>85D</td>
<td>hsp 86</td>
<td>86KD hsp</td>
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**Heat shock polypeptides are grouped into major families**

On the basis of molecular weights and other functional properties, the different heat shock polypeptides in
Fig. 3. Autoradiograms of 3H-thymidine labelled polyoma chromosomes from brain shocked salivary glands of D. melanogaster and D. hydei.

(a) to show specific transcriptional activity of heat shock induced puff; (b) heat shock (37°C for 10 min); (c) salivary gland was labelled with 3H-thymidine for 10 min, then lift-off preparation were autoradiographed to identify (by presence of characteristic dense silver grains) the sites of 3H-thymidine incorporation or active transcription. The differences chromosome arms and the heat shock puff sites are marked. Although the chromosomes and the puff sites are shared differentially in the two species, it is known from other evidences that the sites of heat shock puffs are homologous between these species. Among the differences heat shock puff sites, some are more labelled (more active in RNA synthesis) than others. Heat shock labelled part of the general chromosomes transcription so that most of the chromosome regions (other than heat shock puffs sites) are lesser labelled. The autoradiograpy continues to be active in RNA synthesis as evidenced by its very heavy labelling, are obvious chromatin where all chromosomes remain attached.

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diverse organisms have been grouped into 4 major families: the hap 90 family, hap 70 family, hap 60 family, and the low mol. wt. hap family.

In Drosophila, the hap 90 family is represented by the 83kd hap with an gene being located at 63BC put site. This is the only heat shock protein gene in D. melanogaster which has an isomorph and requires aplication. The 83kd hap gene is also expressed without heat shock in a developmentally regulated manner. The hap 70 family is represented by 58kd and 60kd haps. Hap 70 is the most abundant among induced haps and is also the most highly conserved in all organisms. In D. melanogaster, there are multiple gene copies for hap 70, with at least 2 copies at 81A and three at 87C locus. In addition, there are a number of other genes that code for polypeptides related to hap 70 in its sequence but which are expressed under non-heat shock condition (constitutive expression). These hap-related proteins are termed heat shock cognates (hsc 70 for hap 70 related polypeptides). The gene for hap 68 is located at 95D puff site and shows some homology with the hap 70 genes. However, the induction of hap 68 is much less compared to that of hap 70.

The low molecular weight hap family in D. melanogaster is represented by 4 polypeptides, the 27kd, 26kd, 23kd and 22kd haps. The genes for these four polypeptides and for three other heat inducible transcripts are clustered within a 11kb DNA sequence at the 67B puff site. All these polypeptides share some homology with each other and with the hsc 70. The 23kd hap appears more prominently induced by heat shock than the other three of the low mol. wt. hap family. All the low mol. and wt. haps are also expressed without heat shock in a developmentally regulated manner. They show a complex pattern of cell type and developmental stage-specific regulation by eddygene.

In addition to the above well-known haps, a 74kb histone, H2B variant, is also known to be heat-inducible in D. melanogaster (Fig. 2). The polypophenitin gene, coding for tandem repeats of ubiquitin mRNA and located at 63F site is also heat inducible. A 30kd polypeptide has also been reported in several studies to be heat inducible but not much is known about this polypeptide.

So far nothing is known about products of heat-inducible genes located at 33B, 58F of 70A puff sites. These sites were identified as minor heat shock puffs due to formation of small sized puffs in response to heat shock (Ashburner, 1970).

A heat shock polypeptide with molecular weight around 60kd has been seen in bacteria (the 58kd goat polypeptide of E. coli), plants and many animals. In plant and animal cells this 60kd family hap has been localized to wisp mitochondria and chloroplasts (McMullin and Halberg, 1988), although it is product of a nuclear gene. A 60kd family hap was so far not known to exist in Drosophila. However, Lakhotia and A.K. Sinha recently (1989) reported induction of a 58kd hap in Malpighian tubules of Drosophila more recently, using western blotting this 58kd polypeptide has been found (Lakhotia and Blupenda, N. Singh, unpublished) to be homologous to the 60kd hap known in other organisms.

Some heat shock genes in Drosophila do not make any HSP There are two other heat shock genes, the csp - repeat sequence and the 95D locus which are different from the rest. The so-called csp repeat sequences are interspersed with hap 70 coding sequences at the 87C puff site and are heat inducible. Similar sequences present elsewhere in the genome, however, are not heat inducible. The heat inducible csp repeat sequences make abundant transcripts when heat shocked but these transcripts are not translated (Lengyel and Graham, 1954). Functions of these heat inducible csp repeat sequences are not clear. It is also intriguing that though similar csp sequences are present at 87C locus of D. simulans, a sibling species of D. melanogaster, these are not heat inducible.

The 93D heat shock locus of D. melanogaster is an unusual gene

The heat shock locus at 93D site is unique among all heat shock genes of D. melanogaster. This is ide-
tilded as a major heat shock puff site due to its large size and a higher level of 3H-uridine incorporation (Ashburner, 1970; Mukherjee and Lakhota, 1979). This puff is also uniquely inducible with benzamide, colchicine, thiourea, etc. without consistent in-
duction of any of the other heat shock puffs (see review by Lakhota, 1987, 1989). Lakhota and Mukherjee (1982) found that the singular transcriptional induction of the 92D puff by benzamide etc. was not correlated with appearance of any novel polypeptide in such cells. In another study, Lengyel et al. (1980) had shown certain other unusual properties of the RNA transcribed at the 93D locus. Considering these ob-
vervations, Lakhota and Mukherjee (1982) suggested that the transcripts of 93D are not translated. This was subsequently confirmed by a direct analysis of the base sequence of this locus (see Lakhota 1987, 1988; Par
due et al., 1990). The 92D locus, called har2 2 heat shock RNA genes, Bandem et al. 1989), makes three major transcripts: the largest is about 1.2kb long while the other two are 1.5' and 1.2kb long, respectively. These are present in all cells at the time but their relative levels increase following the heat shock. The transcribed part of the har2 gene includes a 5' region which is unique and a 3' region consisting of tandem repeats of a 260bp sequence extending over 10-12kb long stretch (this repeat sequence is unique to this locus). The 1.2kb transcript covers the entire length of har2 while the 1.9kb transcript represents only the proximal part including an intron of ~700bp. The 1.9kb transcript is processed to yield the 1.2kb RNA. All species of Drosophila have a 92D-homolog identified on the basis of specific inducibility with benzamide, colchicine etc. (Lakhota and Singh, 1982). These homologous loci in different species show similar genomic organization and expression to the size and location of the two exons and the intron and in having a long stretch of repeat sequences at the 3' end (review by Lakhota, 1987, 1989; Parndue et al., 1990). As discussed later, heat shock genes are remarkable for conservation of their function and base sequence. Similar genomic organization and inducible properties of the har2 gene in different species of Drosophila etc. are in agreement with the general conservation of heat shock genes. However, it was very surprising to find that the primary base sequence of the transcribed part of har2 gene showed very rapid sequence divergence so that even closely related species do not share much base sequence homology in this locus. It is also in-
triguing that in spite of its apparently non-coding transcripts and its rapid sequence divergence in related species, this gene is essential for normal survival of the fly since complete deficiency of this locus leads to considerable larval lethality and almost complete adult lethality (Lakhota, 1988). Apparently, the har2 gene functions without a protein product. At present it is believed that a large 1.2kb transcript, localized to the nucleus, has protein-binding properties for its regulatory functions while the smaller and cytoplasmic 1.2kb transcript somehow monitors "health" of the translational machinery of cell (Bendena et al., 1989; Lakhota, 1988; Parndue et al., 1990).

Heat Shock Response is Universal

A most remarkable revelation of the very early studies on heat shock induced puffing changes was that all species of Drosophila showed heat shock puffs on chromosomally homologous regions (Fig. 3): this sug-
gested that the gene loci responding to this cellular stress were also homologous. The initial observations on protein synthesis in various stages of different developmental stages in several species of Drosophila also revealed striking similarities in the molecular weights of the new polypeptides induced by heat shock (Tissiares et al., 1974; Lewis et al., 1975). These initial observations suggested that the response to thermal stress was similar in different cell types of Drosophila, notwithstanding their otherwise highly specialized ac-
tivities. Search for heat shock induced changes in protein synthesis in diverse organisms, initiated soon after the discovery of heat shock proteins in Drosophila, quickly confirmed universality of the heat shock response. The cellular response to thermal and related stresses was found to be remarkably similar in all organisms from bacteria to man (Selleslenger et al., 1982). With the advent of recombiant DNA techni-
cues, heat shock genes from different organisms were

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cloned and sequenced. The most important aspect to emerge from these studies was that the heat shock genes are highly conserved and that all cell types of all organisms generally respond in a similar fashion to thermal stress. As an example of the evolutionary conservation of heat shock genes, it may be noted that the hsp70 genes of pro- and eukaryotes show about 50 to 70% homology. In all organisms, the heat shock polypeptides can be grouped into the four major (the 90k, 70k, 60k and the low mol. wt.) families mentioned earlier. Among these, as in the case of Drosophila, the hsp70 is always the most abundantly induced after heat shock.

It was also seen that a Drosophila heat shock gene when placed in mammalian cells, would be induced by heat shock at a temperature at which the host mammalian cells experience heat shock. This is interesting since while 37°C is normal for mammalian cells it is a strong heat shock condition for Drosophila; therefore, one may have expected that a Drosophila heat shock gene when placed in mammalian cells should always be under thermal stress and should remain induced. However, what was seen was that the Drosophila heat shock gene in mammalian cells responded to heat shock only along with the host’s heat shock genes at 42°C–43°C. Experiments of this kind thus showed that not only the heat shock genes were conserved, their regulation was also conserved through evolution and that something else than the gene itself detects thermal stress in cell.

The heat shock response can be modulated by developmental and environmental conditions. While the heat shock response is generally universal for all cell types of all organisms, a few situations are known where the response to thermal stress may vary in relation to specific cell type, developmental stage and other conditions of development. Very early embryonic cells are usually unable to mount a heat shock response. Certain stages of gametogenesis in some animal groups also have been found to be unable to allow heat shock induced synthesis of hsp’s. It has been shown that development of Drosophila larvae at 15°C specifically affects synthesis of hsp23: heat shock to such larvae fails to induce synthesis of hsp23 while other hsp’s are induced in the usual fashion (Lakhotia and Singh, 1988). Another interesting feature of the heat shock response is that the temperature which is sensed by the cells as strong heat shock is relative to the temperature at which the individual organism was growing; it was seen that Chironomus larvae (dipteran larva coloured red due to hemoglobin in their blood) growing in water at temperature > 33°C (as happens during summer months) do not suffer a strong heat shock at 37°C while the same larvae if grown at 24°C (in laboratory or during winter months) would already experience heat shock at 33°C (Nath and Lakhotia, 1989).

In the context of global nature of the heat shock response, it is remarkable that the Malpighian tubules of Drosophila respond to heat shock by synthesizing a very different set of proteins; Lakhotia and Singh (1989) recently reported that while none of the usual hsp’s was synthesized in Mspaghian tubules of Drosophila larvae following a heat shock, an entirely different set of polypeptides, the Malpighian tubules specific hsp’s, was induced by the thermal stress. This observation opens a new dimension to nature and mechanism of the heat shock response.

Mechanism of Heat Shock Response

Soon after discovery of the heat shock response in Drosophila cells, it was found by Sin (1975) that microinjection of mitochondria extracts of heat shocked cells into polytene cells of non-heat shocked salivary glands of D. melanogaster caused induction of heat shock peels. Thus the heat shock genes themselves were not directly raising elevated temperature, rather the thermal stress brought about certain changes in cell which in turn stimulated the heat shock genes to transcribe. Earlier mentioned experiments on expression of Drosophila heat shock genes in mammalian cells also agreed with this. It is now well known that all heat-inducible genes in all organisms carry more than one copy of a 13bp consensus sequence, GAA/TTC/AGA/AA/TTC (a is any base), upstream of
their transcribed region. This 14bp sequence is termed the heat shock element (HSE) or heat shock promoter and is responsible for heat shock induced transcription of the gene. Recent studies show that the core HSE is only a 10bp sequence (aTTCanGAAn), an inverted repeat of the 5 base pair, nGAAAn (Schlesinger, 1990; Nagao et al, 1990). The transcriptional activation signal is dependent upon binding of an active heat shock transcription factor (HSTF or HSF) with one or more of these upstream HSEs. Every cell is believed to carry the HSTF protein in an inactive form so that it cannot bind with the HSEs. However, heat shock and some other stress conditions bring about certain changes in the HSTF so that it is activated and can bind with the HSEs which in turn promote active transcription of the downstream gene. Genes for Yeast and Drosophila HSTF have been cloned and a comparison of these shows that the HSTF gene has not been as strongly conserved as the heat shock genes and their HSEs. Nevertheless, it is apparent that the HSTF of one species is able to identify the HSE on another species’ heat shock genes.

Biological significance of the heat shock response and functions

The remarkable conservation of the heat shock response in all organisms (prokaryotes, plants and animals) suggests that the heat shock genes evolved very early in the history of life and their cellular functions under conditions of thermal and other stresses are of vital importance. Soon after the discovery of heat shock response, it was shown that Drosophila larvae or flies briefly exposed to a milder heat shock at 33°C could survive better a severe heat shock at 39°C, which otherwise would be lethal (Lindquist, 1986). These and other similar studies in Drosophila and other organisms revealed that the heat shock response was involved in thermoprotection and in development of thermostolerance. It was also seen that if RNA and/or protein synthesis was inhibited during the period of milder heat shock, thermostolerance did not develop. Similarly at the cellular level, if syntheses of heat shock protein was inhibited during exposure to 37°C, the cells did not resume normal protein synthesis when returned to 25°C. It was clear from these experiments that the heat shock proteins somehow help the cell escape deleterious effects of elevated temperature. Although full details are still not clear, significant progress has been made in recent years in elucidation of the cellular activities of the various hsp families (see reviews, see Pelham, 1980; Lindquist, 1988; Lindquist and Craig, 1988; Nagao et al, 1990; Schlesinger, 1990).

Members of the hsp70 family are involved in translocation of various proteins across eukaryotic cell or gannelle membranes, including the endoplasmic reticulum, chloroplast and lysosome: it is proposed that hsp70 functions as a molecular chaperone by unfolding the partially folded polypeptides so that they can be translocated through a membrane pore. In the presence of ATP, hsp70-like proteins have been shown to bind and to dissociate protein complexes.

The hsp90 family proteins also complex with polypeptides and have ATPase activity. However, in contrast to the disassembly and unfolding function of the hsp70, the hsp90s are involved in folding and assembly of polypeptides in mitochondria and chloroplasts.

The hsp90 family of proteins are abundant in normal cell cytoplasm and form complexes with a wide variety of other proteins, like glucocorticoid and other steroid hormone receptors, several kinases, tubulin actin etc. In summary, the hsp90, hsp70 and hsp60 family of proteins protect, preserve and recover the functions of various other proteins (Schlesinger, 1990). Another heat shock protein, the ubiquitin-protein function in protein degradation. In the course of normal proteolytic turnover in cells, the proteins to be degraded are flagged by ubiquitin-binding. Heat shock also leads to thermal denaturation of many proteins which could be toxic if not immediately removed. It is in this process that the product of the heat-inducible polyubiquitin gene participates. I agreement with this is the observation that polyubiquitinated proteins increase about 2-fold in heat shock
ed cells which are subsequently removed by ubiquitin-dependent proteolytic destruction.

The low red. wt. family hps seem to have a structural role since they are abundant in normal cells also (Nagata et al., 1990). In Drosophila and other systems, it has been shown that these proteins form large aggregates during heat shock, that these aggregates concentrate in perinuclear regions and that they are tightly associated with normal cellular mRNAs. This association may help protect the normal cellular mRNAs which are not being translated during heat shock (Arigo, 1987; Leicht et al, 1986; Nover et al. 1989).

A new dimension to studies on heat shock response has been added by recent discoveries that these are dominant antigens of infectious microorganisms and that a significant fraction of microbial infection induced immunoglobulin and cytoprotective T helper cells is directed against peptides derived from hps. Both the invading microorganisms and host cells suffer stress during infection and thus produce hps which stimulate the immune response. However, since uninfected host cells also contain hps, there is a risk of autoimmune responses: cases of autoimmune disease involving hps are known (see Lydyard and van Eden, 1990; Schedelinger, 1990).

Concluding Remarks

Initial studies on the heat shock response in Drosophila provided a very useful experimental approach to correlate morphological pufgling of polytene chromosomes with synthesis of specific mRNAs and corresponding proteins. Even since then, studies on hsp70 genes and heat shock proteins in very diverse organisms are continuing to provide new insight into gene regulatory and cellular adaptive processes.

In addition to the heat shock paradigm being extensively used for studies on organization, expression and regulation of genes, Drosophila geneticists have also made novel and a very fruitful use of the knowledge gained from studies on regulation of heat shock genes: a variety of chimeric genes have been synthesized in vitro where the coding sequence of a given gene is placed downstream of a heat shock promoter and the fusion gene put back in Drosophila genome using F-element mediated germine transformation (for details of this, see the article on "New approaches in Drosophila Genetics" in this issue). This strategy permit in vivo activation of that gene and when required by applying heat shock to such transformed individuals (see "Demonstration of heat shock induced gene activity in transgenic Drosophila melanogaster with a reporter gene fused to a heat shock promoter" in this issue).

Particular interesting examples of this approach are recent studies in which some homeo-box containing genes (for details of homeotic genes and homeo-box, see the article on "Genetics of Body-Pattern Formation During Embryonic Development in Drosophila" in this issue) of human or mouse origin were combined with hsp70 promoter of Drosophila and the fusion gene inserted in Drosophila genome; when activated with heat shock, the human or mouse homeotic gene did the same function in Drosophila as was expected from their molecular homology to corresponding Drosophila homeotic genes (Malicki et al., 1990; McGinnis et al, 1990).

Elucidation of molecular details of the role of diverse heat shock gene products in normal cell and under conditions of stress is progressing very fast and one would expect that within the next few years the biological significance of this very ancient adaptive response would be clearly understood.

References


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