Foreword

Environmental factors, cellular stress and evolution

For its survival and continuity, an organism has to be "in tune" with its internal as well as external environment, neither of which is ever static. Consequently, the organism and its constituent cells incessantly adjust their physiological milieu to remain in harmony with the dynamic environment. The adjustments involve long-term evolutionary adaptations as well as short-term responses to sudden changes. The sudden changes in environment are stressful to cells and since the nature of changes experienced by organisms are enormously varied, one may expect the cellular responses to be equally varied. Surprisingly, however, work carried out during the 1960s and 1970s revealed that the core response of individual cells to a variety of biotic and abiotic environmental stresses is remarkably conserved. For historical reasons, this cellular response has come to be known as the heat shock response.

Intensive studies of genes and proteins induced by cellular stresses have provided deep insights not only into some of the basic cellular processes like protein folding, gene regulation, cellular homeostasis and so on, but have also stimulated biotechnological and clinical applications. At a more fundamental level of biology, it is clear that environmental stress factors have been key players in shaping organic evolution. However, research on the molecular biology of stress responses has often remained separated from that on the role of environmental (stress) factors in evolution and development. It is obvious that an integration of these diverse domains is essential for a comprehensive understanding of the biology of living organisms as well as for improvements in practical applications of our understanding of the stress responses. An international meeting was held at the Banaras Hindu University, Varanasi in October 2006 (figure 1) to provide an integrated perspective for understanding the roles of stress proteins and stress responses in cellular homeostasis and evolution. This meeting was a sequel to several earlier meetings on related themes: at Varanasi in 1997 (*J. Biosciences*, 1998, vol. 23, No.4), at Wuhan in 1999 (*Biology International* 2001, vol 40, pp 1-36), at Quebec in 2003 (*Biology International* 2004, vol 45, pp 34-49) and at Cairo in 2004 (*J. Biosciences* 2004, vol 29, No. 4, pp. 447–511).

The twenty papers in this issue are based on the presentations at the October 2006 meeting at Varanasi (Lutz Nover of Frankfurt presented a talk on "Multiplicity of heat stress transcription factors controlling the complex heat stress response of plants" but could not submit a manuscript; M Evgenev of Moscow could not attend the meeting but has contributed a manuscript for this issue).

Martin Feder while discussing the need and means for achieving an integrative perspective of cellular stresses, highlights the necessity of resolving three fundamental issues: (i) Is variation in nucleotide sequences, genes, gene products, etc., seldom, commonly, or always consequential for stress resistance? (ii) Does environmental stress reduce or enhance genetic variation, which is the raw material of evolution? (iii) Is the present distribution of organisms along natural gradients of stress largely the result of organisms living where they can, or is adaptive evolution generally sufficient to overcome stress?

The paper by Korcsmaros *et al* highlights the integrative and strategic roles played by stress proteins in normal as well as stressed cells through their functioning as "weak-links" in cellular networks.

The next six papers (Sørensen and Loeschecke, Salathiya and Queitsch, Brakefield *et al*, Dahlhoff and Rank, Evgen'ev *et al* and Beck *et al*) inter-relate environmental factors, stress proteins and their genes, the development of organisms and evolutionary forces in natural populations. These studies make it clear that what we learn from model organisms under "comfortable" laboratory conditions does not always reflect what happens out in the field where conditions are continuously changing and unpredictably hostile. The gene pool in wild populations is also not homogenous. This means that the response to stresses and the genomic buffering capacity to meet variable conditions become significant forces in shaping evolutionary directions. With the availability of advanced tools of genomics, proteomics and developmental genetics, the relationship between canalization, developmental plasticity and stress proteins (or molecular chaperones) is turning out to be a fascinating one. Further elucidation of cellular stress responses in the context of "Evo-devo-eco Biology" should be very exciting indeed.

Figure 1. Speakers at the International symposium on "Environmental Factors, Cellular Stress and Evolution" held at the Banaras Hindu University, Varanasi from October 13, 2006 to October 15, 2006.

Söti and Csermely examine the role of stress proteins/molecular chaperones in ageing and degenerative diseases from the perspective of overload of damaged proteins in cells. Neckers emphasizes the need for a better understanding of the biology and biophysics of the ubiquitously present Hsp90 to facilitate development of target-specific drugs to fight cancer and neurodegenerative disorders. Likewise, Kumar *et al* consider the structure of the Hsp90 of the malarial parasite, *Plasmodium falciparum*, as a prelude to developing appropriate drugs for its control. Recent studies have revealed interesting roles of stress proteins in modulating neurodegenerative diseases caused by expansion of poly-glutamine stretches. In view of these observations, Bettencourt *et al* have raised a pertinent question about the possible roles of polymorphism in poly-glutamine stretches in shaping biological fitness via modulating the levels of stress proteins in natural populations of *Drosophila*.

Schumann, Prasad *et al* and Sadhale *et al* examine aspects of regulation of stress responses in pro- and eukaryotes. As discussed by Schumann, the sensors that trigger the heat shock response in bacteria can be the titration of molecular chaperones by damaged proteins or proteases which keep either a positive transcriptional regulator inactive or a negative regulator active or do not attack the regulator, respectively, under physiological conditions. Prasad *et al* have compared the organization and expression of the cyanobacterial Kdp system involved in regulating the potassium balance in cells and thus with critical roles in bacterial stress responses. Sadhale *et al* compare the transcriptional regulation of heat shock genes in prokaryotes and eukaryotes and argue that as in prokaryotes, eukaryotes also have a common functional unit in the transcription machinery through which the stress specific transcription factors regulate the rapid induction of specific genes in stressed cells; they point to some candidates that may be the eukaryotic equivalent of bacterial sigma-s factors.

The most conventional and popular view of heat shock proteins is of intracellular proteins involved in the chaperoning of other proteins. This simplistic view is no longer valid. As highlighted by Asea, stress proteins may also function as "danger signals" when secreted outside the cell. He discusses the mechanism of secretion of the stress-inducible HSP72 in serum and its role in immune response.

Kolla *et al* and Arya *et al* consider the roles of heat shock factors and heat shock gene products, respectively in apoptosis. Kolla *et al*. show that in a rat histiocytoma cell line, the two heat shock factors HSF1 and HSF2 regulate heat shock response and autophagy in a complex manner. Unlike in other cells, HSF1 fails to acquire DNA-binding activity in these cells following heat shock; on the other hand, compromising HSF2 activity inhibits the characteristic heat shock-induced autophagy displayed by the rat histiocytoma cell line. Arya *et al* survey the intricate cross-talk between different heat shock proteins and apoptotic factors which decides in a subtle manner the survival or death of a cell. They also suggest that compared to the stress proteins functioning as "weak links" in cellular networks, stress-induced non-coding RNAs, like the hsrω transcripts in *Drosophila*, can function as hubs and thus be high up in the hierarchy of cellular networks.

Finally, the two papers by Batra *et al* and Verma *et al* exemplify biotechnological applications of stress proteins in developing stress-tolerant rice varieties.

The articles in this issue provide succinct surveys of their chosen fields. They will be of immense benefit not only to specialists but also to those generally interested in the broad area of Stress Biology. This Special Issue will have served its purpose if it catalyzes the integration of stress responses with evolution and environmental factors.

I take this opportunity to thank all the contributors, who were very cooperative in contributing manuscripts in time, the reviewers who responded quickly with their detailed comments and the office of *Journal of Biosciences* for its help.

Subhash C Lakhotia
Cytogenetics Laboratory,
Department of Zoology,
Banaras Hindu University,
Varanasi 221 005, India
(E-mail, lakhotia@bhu.ac.in)