In the first *Highlighted Topics* article featured in this issue of the *Journal of Applied Physiology*, “Hypothermic protection of the ischemic heart via alterations in apoptotic pathways as assessed by gene array analysis” (pages 2200–2207), Ning and coauthors explore the modulation of various signaling pathways in a perfused rabbit heart model with a cDNA array and semiquantitative RT-PCR experimental approach. Protection can be proffered by application of cold during ischemia, which has been reported since the 1950s and is widely used in cardiac surgery. Recently, it has been demonstrated that hypothermia applied before warm ischemia also induces protective adaptive responses in the reperfusion period. This adaptation is characterized by enhanced postischemic gene expression for specific stress-related and mitochondrial constitutive proteins with a threshold phenomenon (30°C). Although some hypothermia-induced protection can be attributed to changes in energy utilization and supply, other injury-reducing mechanisms may also operate. However, the protective mechanisms for hypothermia against ischemic injury in the heart still elude our understanding. In the present study, Ning and colleagues examined expression of 302 genes from seven functional pathways in hearts exposed to hypothermic or normothermic ischemia. Mild hypothermia (30°C) modified postischemic gene expression, while preserving cardiac function. Eight of the thirteen modified genes related to apoptosis pathways. In particular, hypothermia blunted postischemic expression of transformation-related protein 53 (tumor suppressor) and its target genes, such as Gadd45 and Gadd45-β that have not been previously implicated as cell death mechanisms in cardiomyocytes. Thus the cDNA arrays identified a novel pathway possibly related to ischemic injury in the heart and its regulation by temperature. In addition, this study highlights the complex and multifaceted nature of hypothermic protection and adaptation in the heart, including tolerance to hypoxia-induced aerobic pathway impairment, attenuation of byproduct accumulation, and maintenance of mitochondrial membrane stability. Furthermore, this study may provide a clue to a potential novel approach for protection in hypoxic conditions, such as patients undergoing cardiac surgery or treatment in a high-altitude environment or tissue cryobiological preservation and rejuvenation.

The second *Highlighted Topics* article in this issue, “Effect of acute heat shock on gene expression by human peripheral blood mononuclear cells,” by Sonna and colleagues (pages 2208–2220), applied gene chip array technology (by using an array containing ~12,600 sequences representing over 11,500 genes) to identify changes in gene expression that occurred in human peripheral blood mononuclear cells 160 min after a conventional in vitro heat shock (43°C for 20 min). In addition to heat shock proteins and chaperonins/cochaperonins, the authors identified over 300 sequences that showed a statistically significant two-fold or greater change in expression as a result of heat shock. Interestingly, these not only included members of every functional class previously known to be part of the cellular response to heat stress but also many sequences not previously known to be involved in the heat shock response. This study represents one of the most extensive surveys performed to date of heat-induced changes in gene expression by normal (i.e., nontransformed) human cells. The results demonstrate that the human gene expression response to heat stress (reviewed in the April 2002 issue of the *Journal of Applied Physiology*) is even broader than previously realized and suggest that heat stress-induced changes in gene expression may have effects even on pathways traditionally considered to be regulated primarily at the level of protein function, such as the mitogen-activated protein kinase pathways.