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Cellular responses to mild heat stress

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Since its discovery in 1962 by Ritossa, the heat shock response has been extensively studiedby a number of investigators to understand the molecular mechanism underlying cellular responses to heat stress. The most well characterized heat shock response is induction of the heat shock proteins that function as molecular chaperone and exert cell cycle regulatory and anti-apoptotic activities. While most investigators have focused their studies on the toxic effects of heat stress in organisms such as severe heat stress-induced cell cycle arrest and apoptosis, the cellular response to fever-ranged mild heat stress has been rather under-estimated. However, the cellular response to mild heat stress is likely to be more important in a physiological sense than that to severe heat stress because body temperature of homeothermic animals increases by only 1~2°C during febrile diseases. Here we show that mild heat stress plays a beneficial role(s) in organisms through 1) facilitating growth factor-mediated cell survival and proliferation, 2) modulating cell death mode, via intracellular signal transduction cascades including the receptor tyrosine kinases (RTKs)-Ras-Rac1, PI3K-Akt/PKB, and ERK1/2 and p38MAPK signal pathways. Based on these results, we suggest that mild heat stress may act as one of physicochemical signals that regulate activities of membrane proteins through affecting membrane fluidityand thereby activate different set of intracellular signal pathways to reprogram gene expression for survival in organisms, in a similar fashion to reactive oxygen species (ROS) that modulates the activities of proteins, via oxidizing specific redox-sensitive sulfhydryl group. We further suspect thatmild heat stress and ROS may be evolved as primitive signal molecules at the early stage of evolution before growth factor-mediated cell growth machinery is established. Further studies may provide new insights into theelucidation of molecular mechanism for fever-dependent cell regulation in organisms.