Hyperthermia (208-212)

208  Inhibition of Aggregate Formation of Mutant Androgen Receptor by Molecular Chaperones
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Molecular chaperones are known to be able to inhibit the aggregate formation of partially denatured proteins and refold them. Also, overexpression of molecular chaperones can correct the misfolding of some mutant proteins. Spinal and bulbar muscular atrophy (SBMA) is inherited neurodegenerative disease and one of the triplet repeat diseases. It is caused by the expansion of an unstable CAG repeat in the coding region of androgen receptor (AR). Here, we report the inhibitory effect of molecular chaperones on the aggregate formation of mutant AR.

Transfection of mutant AR (97 CAG repeat) into Neuro2a cells resulted in the aggregate formation in the cell and induced apoptotic cell death. Cotransfection of Hsp70 or Hsp70/Hsp40 with mutant AR significantly suppress the aggregate formation and subsequent apoptosis. In contrast, Hsdj alone or Hsp70/Hsdj has no apparent effect on the aggregate formation of mutant AR. Also, in vitro experimental system, Hsp70 or Hsp70/Hsp40 has inhibitory effect on the aggregate formation of truncated mutant AR (65 CAG repeat). These results suggest that molecular chaperones can be used for the protection and therapeutic treatment of the diseases caused by protein misfolding.

209  Activation of Mitogen Activated Protein Kinases by Heat Shock

It has been well known that tumor-derived cells are more sensitive to heat than normal cells. However, the mechanism of differential heat sensitivity of these cells are still unknown. We investigated activation of extracellular signal-regulated kinases 1 and 2 (ERK1/2), c-Jun amino terminal kinases 1 and 2 (JNK1/2), and p38 in normal human embryo (HE49) cells and in human colon cancer cells (RKO) heated at 43 °C, using phosphorylation specific antibodies. We found that ERK1/2 were phosphorylated after heat shock neither in HE49 and RKO, but the kinetics of ERK1/2 phosphorylation in HE49 was different from that in RKO. JNK1/2 were phosphorylated in heat shock treatment in RKO, but not in HE49. p38 was not phosphorylated after heat shock neither in HE49 and RKO. These data indicate that the effect of heat shock on activation of MAP kinases is different between normal human cells and tumor-derived cells. This difference might explain the differential sensitivity of these cells.