

Human Embryonic Stem Cells Experience a Typical Apoptotic Process upon Oxidative Stress

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Embryonic stem (ES) cells, derived from preimplantation embryos, are able to differentiate into various types of cells consisting the whole body, or pluripotency. In addition to the plasticity, ES cells are expected to be different from terminally differentiated cells in very many ways, such as patterns of gene expressions, ability and response of the cells in confronting environmental stimulations, metabolism, and growth rate. As a model system to differentiate these two types of cells, human ES (hES, MB03) cells and terminally differentiated cells (HeLa), we examined the ability of these two types of cells in confronting a severe oxidative insult, that is H₂O₂. Ratio of dying cells as determined by the relative amount of dye neutral red entrapped within the cells after the exposures. Cell death rates were not significantly different when either MB03 or HeLa were exposed up to 0.4 mM H₂O₂. However, relative amount of dye entrapped within the cells sharply decreased down to 0.12% in HeLa cells when the cells were exposed to 0.8 mM H₂O₂, while it was approximately 54% in MB03. Pretreatment of cells with BSO (GSH chelator) and measurement of GSH content results suggest that cellular GSH is the major defensive mechanism of hES cells. Induction of apoptosis in hES cell was confirmed by DNA laddering, induction of Bax, and chromatin condensation. In summary, hES cells 1) are extremely resistant to oxidative stress, 2) utilize GSH as a major defensive mechanism. and 3) experience apoptosis upon exposure to oxidative stress.

Key words) *Oxidative stress, hES cell, GSH, Apoptosis*