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RATANA BANJERDPONGCHAI : THALASSEMIC SERA AND APOPTOSIS OF HUMAN UMBILICAL CORD VEIN ENDOTHELIAL CELLS. THESIS ADVISORS: PRAPON WILAIRAT Ph.D., AHNOND BUNYARATVEJ Ph.D., MATHUROSE PONGLIKITMONGKOL Ph.D., SUKATHIDA UBOL Ph.D., KOVIT PATTANAPANYASAT, Ph.D. 247 p. ISBN 974-589-073-1

Programmed cell death or apoptosis is a mode of cell death which occurs in both physiological (such as the shedding of epithelial cells in gastrointestinal tract or the peeling of skin) and pathological processes (for instance, in cancer, autoimmune diseases and acquired immune deficiency syndrome). It has been reported that when human umbilical cord vein endothelial cells (HUVECs) were incubated with α- or β-thalassemic serum, the cells floated and the number of proliferating cells were decreased (Bunyaratvej A et al. Southeast Asian J Trop Med Health 1992; 2:105). The aim of this work was to demonstrate the type of cell death (apoptosis or necrosis) and to determine the mechanism or the mediator involved.

It was found that the HUVECs when treated with thalassemic serum or extracted LDL, died via the apoptosis pathway. This was based on a number of morphological criteria, viz. condensation of nuclei and cytosol, membrane blebbing, margination of nuclear matrices, and the appearance of apoptotic bodies. It was also based on biochemical evidence of high molecular weight DNA (50-300 kb) in pulse field gel-electrophoresis in the early phase of apoptosis of DNA and ladder pattern (DNA cleavage into multiple of nucleosomes containing 180-200 bp) on agarose gel-electrophoresis in the late phase. Cleavage of nuclei DNA was also confirmed by using terminal deoxynucleotidyl transferase (TdT)-mediated dUTP-fluorescein nick end labeling (TUNEL) assay. Another property of apoptotic cells included the movement of the anionic phospholipid, phosphatidylserine, from the inner to the outer layer of cell membrane, which was detected by flow cytometry using annexin V-FITC. One of the mechanisms involved, namely *de novo* protein synthesis, was shown by the inhibitory effect of cycloheximide.

Since oxidative stress exists in thalassemic serum, this could be a candidate to cause HUVEC to undergo apoptosis. One culprit could be LDL extracted from thalassemic plasma which might be in an oxidized or acetylated form. This work has clinical implications for the vascular system and demonstrates how one might provide treatment for such thalassemic patients.