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THAWATCHAI LERTWORASIRIKUL : DYSERYTHROPOIESIS AND ERYTHROID APOPTOSIS ASSOCIATED WITH PLASMODIUM FALCIPARUM MALARIA : *IN VITRO* STUDY OF MUTUAL EFFECT BETWEEN CELL POPULATIONS. THESIS ADVISORS : TONGTAVUCH ANUKARAHANONTA, M.D., Ph.D., AHNOND BUNYARATVEJ, Ph.D., KOVIT PATTANAPANYASAT, Ph.D., SOMPHONG SAHAPHONG, M.D., Ph.D., SUDA RIENGROJPITAK, Ph.D. 123 P. ISBN 974-664-382-7

It has been suggested that ineffective erythropoiesis plays an important role in anemia associated with malaria other than destruction of infected red cells; however its underlying mechanism remains unclear. The present study proposes a co-culture system which provides a simple way for monitoring the mutual effect between cell populations. The co-culture system incorporated erythroblasts, macrophages and *Plasmodium falciparum* malaria-infected red cells into one- and two-compartment units indicating direct and indirect contact between cell populations, respectively. Instead of infected red cells, normal red cells were used in the noninfected control groups. In the two-compartment system, interaction between the two compartments of co-culture system was mediated via soluble factors freely passing through a membrane filter which separated erythroblasts and macrophages from parasitized red cells.

As compared with noninfected conditions, light microscopy of infected conditions revealed a significant number of erythroblasts with dyserythropoietic changes, as manifested by cytoplasmic condensation, membrane blebbing, irregularly-shaped nuclei and karyorrhexis. The infected erythroblasts were also observed in one-compartment systems. Concurrently flow cytometric analysis of annexin V staining related to phosphatidylserine externalization exhibited a population of erythroblasts undergoing apoptosis. A good correlation between two methods was shown. The correlation between parasitemia and TNF- α level suggested the parasite-activated macrophage response which may account for dyserythropoiesis and erythroid apoptosis. These defective effects were partially lessened by the treatments of high dose erythropoietin (EPO) and monoclonal antibodies against human tumor necrosis factor alpha (TNF- α).