3936412 SCPS/M : MAJOR : PHYSIOLOGY; M.Sc. (PHYSIOLOGY)
KEY WORDS : COLONY FORMING UNIT MEGAKARYOCYTE/ INTERLEUKIN-3/ POSTSPLENECTOMIZED THALASSEMIA/ THROMBOCYTOSIS/ THROMBOPOIETIN

LADDA LEUNGRATANAMART: EFFECTS OF THROMBOPOIETIC GROWTH FACTOR ON MEGAKARYOCYTOPOIESIS IN POST-SPLENECTOMIZED THALASSEMIC PATIENTS WITH THROMBOCYTOSIS. THESIS ADVISOR: PAWINEE PIYACHATURAWAT, Ph.D., SUPORN CHUNCHARUNEE, M.D., KULAWEE SUJARIT, Ph.D., 113 P. ISBN 974-661-859-8

Thrombocytosis is a documented complication in postsplenectomized thalassemic patients. High platelet counts might be associated with an increase in the number of megakaryocytes resulting from spontaneous growth, an increase in sensitivity of the megakaryocyte progenitor cells in response to thrombopoietic growth factor and/or an increased production of endogenous growth factor. To elucidate these possibilities, the growth and development of marrow mononuclear cells to generate colony forming unit megakaryocyte (CFU-MK) were investigated in postsplenectomized thalassemic patients (Thal/postsplenec) and compared to those in controls and nonsplenectomized thalassemia (Thal/nonsplenec). All Thal/postsplenec had notably high platelet counts (> 500 x 10^9/l) whereas the platelet counts in Thal/nonsplenec were comparable to those in the controls. By using plasma clot culture method, in the absence of exogenous growth factors, spontaneous growth of CFU-MK was observed only in chronic myeloproliferative disorder (MPD) patients but not in the controls, Thal/nonsplenec, or Thal/postsplenec. In the presence of IL-3 and Tpo, morphological features of the growing megakaryocytic colony of Thal/postsplenec were similar to those in Thal/nonsplenec and the controls in which IL-3 stimulates growth of immature megakaryocytes, whereas Tpo stimulates differentiation and maturation of megakaryocytes. The formation of CFU-MK colonies in response to IL-3 and Tpo stimulation in all groups showed concentration-related effects. Formation of CFU-MK in response to different combinations of IL-3 and Tpo was similar to those cultures containing IL-3 alone, but the size of colony was larger and contained a higher number of multilobular nuclei. The extent of responses in most of Thal/postsplenec was similar to that in Thal/nonsplenec and the controls, except that two cases of Thal/postsplenec gave much higher numbers of CFU-MK in response to IL-3 and Tpo. Therefore, high platelet count found in postsplenectomized thalassemic patients was not associated with spontaneous growth or hyperresponsiveness of the cells to growth factors. However, Tpo levels in both serum and bone marrow in Thal/postsplenec were elevated and higher than in Thal/nonsplenec, MPD and normal controls. The significant elevation of Tpo in Thal/postsplenec might be a major factor which could account for the high platelet counts in these patients.

Therefore, the results suggest that thrombocytosis in postsplenectomized thalassemic patients was due mainly to elevated levels of Tpo. Abnormalities of cells might also contribute to thrombocytosis in some patients.