

成人周邊血液造血幹/前驅細胞在紅血球生成過程中之分化特性研究

The Differentiation Characteristics of Human Adult Peripheral Blood Hematopoietic Stem/ Progenitor Cells in Erythropoiesis

中文摘要

紅血球生成指的是造血幹細胞分化為成熟紅血球的過程，此過程是受到一系列內在及外在細胞因子錯綜複雜的影響，但其分子調控機制仍有待澄清。本研究利用了二階段細胞培養法進行體外紅血球生成實驗，在培養期間持續分析紅血球前驅細胞之表面標幟等，以瞭解成人周邊血液造血幹/前驅細胞在紅血球生成過程中如何受體內 EPO、SCF 等細胞因子調控之細胞分化特性。在此培養系統，我們發現在第一階段 CD34+ 造血幹細胞細胞增殖培養期間，成人周邊血液細胞受到同樣的細胞激素影響，但其增殖能力遠不如臍帶血幹細胞，顯示其細胞原始性之消滅；而在第二階段 CD36+ 紅血球前驅細胞增殖及分化培養期間，如同時給予 EPO 及 SCF 時，成人周邊血液細胞增殖的能力顯著較臍帶血細胞敏感，這可能與成人周邊血液在取得 CD36+ 紅血球前驅細胞之初期時表現較多的 SCF 受體 (CD117) 有關。在分化特性方面，實驗結果顯示無論是成人周邊血液或臍帶血細胞，在培養期間如同時給予 EPO 及 SCF 時，將能延緩紅血球母細胞之分化，且其喚起(re-active) γ -globin 血紅素合成有不同之效率。實驗結果亦顯示，成人周邊血液造血幹細胞其 erythropoiesis kinetic 較臍帶血造血幹細胞來得快。另外，在取得 CD36+ 紅血球前驅細胞之初期，成人周邊血液細胞表現 CXCR4 的細胞也較臍帶血高，且表現時間較短，顯示著細胞動員 (mobilization) 之特異性。本研究利用此一細胞培養模式，針對不同發育階段造血幹細胞在紅血球生成過程中對細胞激素之反應特異性做初步了解，未來將繼續進行紅血球生成過程中基因蛋白體變化之分子檢測，期望得知紅血球生成過程中各基因所扮演的角色，以便有助於了解紅血球生成之分子生理、病理機制及其對策應用。

英文摘要

Erythropoiesis is a multistep process of the pluripotent hematopoietic stem cells differentiate to the mature red blood cells, which is influenced by extrinsic and intracellular environmental elements. However, the molecular regulation mechanism remains to clarify. In this study, we applied an two-stage in vitro erythropoiesis culture system to probe the cytokine effect, such as EPO and SCF, on adult peripheral blood CD34+ hematopoietic stem/ progenitor cells. The culture system produced enriched erythroid progenitors and allowing us to evaluate the differentiation characteristics of human adult peripheral blood hematopoietic stem/ progenitor cells in compare to the cord blood ones. We found that in the first (expansion) stage of the culture system, the proliferation capacity of adult peripheral blood is rather

diminished in compare to the new born cord blood. In the second (differentiation) stage of the culture system, the adult peripheral blood has better proliferation capacity than cord blood while stimulated with EPO and SCF. However, SCF retards both of adult peripheral blood and cord blood erythropoiesis and re-actives the synthesis of γ -globin with different extend. The data also shows that the erythropoiesis kinetics of adult peripheral blood is rather faster than the cord blood. In the other hand, the c-kit receptor (CD117) and CXCR4 expression of adult peripheral blood is higher than cord blood in the day0 of second stage and its expression duration is shorter. These results suggest that hematopoietic stem/ progenitor cells response differently to the same surrounding cytokine stimulation to fit the growth physiological requirement, during the growth of our body from fetus to adult. A further functional genomic study will be need for further understanding the molecular mechanism of erythropoiesis during the body growth.