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Control of terminal erythropoiesis via autonomous physical interactions and contact-mimicking stimuli

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In the bone marrow, erythroblast differentiation and enucleation are mainly regulated by adjacent macrophages. However, some parts of erythroblasts are detached from macrophages, contacting only other erythroid cells. Therefore, we hypothesized that additional unknown factors may also regulate erythroid cells, probably by autonomous physical contacts or secreted factors among erythroid cells. Here, to mimic the in vivo environments, human cord blood-derived erythroblasts were purely cultured at a high density to increase the chances of cell-to-cell contact. We observed a significantly increased erythrocyte production rate and viability. In addition, we newly found several contact-evoked signals such as cell adhesion molecule ICAM-4 and integrin VLA-4 at higher density. We also firstly demonstrated that human erythroblast had a secreted form of ICAM-4. When the recombinant protein ICAM-4 was added to the culture media at the terminal maturation phase, the erythroid cells showed marked decrease in nuclear dysplasia in a dose-dependent manner which was one of the main reasons of low RBC production. These results provide new mechanisms for autonomous control of erythropoiesis by physical contacts or contact-mimicking ICAM-4 signals. These findings could enhance in vitro erythrocyte production efficiency for clinical use by reducing the culture media volume and mimicking in vivo cell-to-cell contacts even in a suspension state by adding recombinant proteins.

Biography

Eun Jung Baek, clinical pathologist, earned her medical degree at Hanyang University School of Medicine and has completed her Ph.D. from the same University. She is the director of departments of Clinical Hematology and Transfusion Medicine at Hanyang University Kuri hospital. She has published several papers about in vitro generation of human red blood cells from hematopoietic stem cells. Her papers were highlighted as a cover and a top story in “Transfusion” journal. In recent years, she has focused on the large scale production of human RBCs for transfusion.

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