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Human Megakaryopoiesis Ex-Vivo: Cell Population Modeling Approach

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ABSTRACT

Megakaryopoiesis is defined by production of mature megakaryocytes (Mks) from hematopoietic stem cells (HSC). The production of platelet, which has an important role in hemostasis and wound healing, from Mks is a complex process. An ex-vivo two-stage protocol including HSC expansion and Mk lineage commitment of human umbilical cord blood cells (hUCB) were established 1 . In the first stage, hUCB cells were expanded in co-culture with the bone marrow human mesenchymal stem cells using a cytokines cocktail pre-optimized for HSC expansion. In the differentiation stage, a serum-free medium supplemented by a cytokines cocktail containing TPO and IL-3 were used. In order to describe the phenotype of cells, a mathematical model was established based on the kinetic of cell expansion and differentiation. Using cell population modeling, which computes the concentration of each subset during the time, can provide significant insight into the limiting steps involved in the protocol and how the interaction of different factors can affect the outcome of megakaryopoiesis process. A set of ordinary differentiation equation (ODE) were used, based on the mass balance, to analyze the proliferation and differentiation of HSC. These ODEs were solved and a general solution for each subset was fitted to the experimental result, using the least square method, to determine the unknown coefficient factors for expansion, differentiation and death of each subset.

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References

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