عنوان مقاله:

Human Pluripotent Stem Cell-Derived Erythrocyte Production Using Small Molecule Chir99021

محل انتشار:

بیستمین کنگره بین‌المللی بیولوژی تولید مثل و پانزدهمین کنگره بین‌المللی سلول های بنیادی (سال: 1398)

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خلاصه مقاله:

Background: Human pluripotent stem cells (hPSCs) includ-ing embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs), have made it possible to produce manipulated he-matopoietic stem cells (HSCs), erythrocytes, and lymphocytes. Specially, iPSCs has the potential to provide the personalized blood cells like universal erythrocytes which can be used to study hematologic disorders and new treatments. Several hP-SC-derived erythrocyte production protocols have been intro-duced based on using feeder (from human or mice) cells and human plasma. Here we defined a feeder-free hematopoietic differentiation system by using small molecule CHIR99021, a GSK3β inhibitor and cytokines replicating hematopoiesis dur-ing development.Materials and Methods: In this study hematopoietic differen-tiation in hPSCs was inducted by CHIR99021 in hypoxic con-dition. Hematopoietic stem/progenitor cells (HSPCs) released from hemogenic sacs after further induction by VEGF, IL-6, IL-3, bFGF, erythropoietin (EPO) and SCF, were then cultured in MethocultH4434 to measure colony forming capacity and the erythroid colonies were then counted. Cells were also char-acterized by RT-PCR, Wright-Giemsa staining and immuno-fluorescence and flow-cytometry.Results: Induction of definitive hematopoiesis pathway in hPSCs and hypoxia result in hemogenic sac-like structures. These hemogenic sacs release CD43+ CD45+ hematopoietic progenitor cells capable of producing erythroid colonies after being cultured in semi-solid methyl cellulose based media. Our data showed that hESCs produced more erythroid colonies than iPSCs (22.5% over 9.5% of total colonies). After being in cy-tokine enriched condition for two weeks, these colonies indicat-ed CD235a+ erythroblasts which were nucleated and showed different stages of maturation by Wright-Giemsa staining.Conclusion: Our findings indicate that erythrocytes can be pro-duced from HSPCs produced in our defined protocol. While having fetal characteristics, showing different cell shapes and low yield that can pose as an obstacle in clinical approaches, these hPSCs-derived erythrocytes can still be used as a source to study and improve our knowledge of erythrocyte develop-ment and the in vitro drug delivery systems as .they are not af-fected by cell number and their lower affinity toward oxygen

کلمات کلیدی:
Erythrocytes, Human Pluripotent Stem Cells (hP-SCs), Hematopoietic Stem Cells (HSCs), Hematopoietic Stem/ (Progenitor Cells (HSPCs