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Derivation of Human NK Cells from T Cell-Derived Induced Pluripotent Stem Cells Using Xenogeneic Serum-Free and Feeder Cell-Free Culture System

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Abstract : The derivation of human induced pluripotent stem cells (iPSCs) from somatic cells by direct reprogramming opens wide perspectives in the regenerative medicine. It means the possibility to develop the personal and, consequently, any immunologically compatible cells for applications in cell-based therapy. The purpose of our study was to develop the technology for the production of NK cells from T cell-derived induced pluripotent stem cells (TiPSCs) for subsequent application in adoptive cancer immunotherapy. Methods: In this study iPSCs were derived from peripheral blood T cells using Sendai virus vectors expressing Oct4, Sox2, Klf4 and c-Myc. Pluripotent characteristics of TiPSCs were examined and confirmed with alkaline phosphatase staining, immunocytochemistry and RT-PCR analysis. For NK cell differentiation, embryoid bodies (EB) formed from (TiPSCs) were cultured in xenogeneic serum-free medium containing human serum, IL-3, IL-7, IL-15, SCF, FLT3L without using M210-B4 and AFT-024 stromal feeder cells. After differentiation, NK cells were characterized with immunofluorescence analysis, flow cytometry and cytotoxicity assay. Results: Here, we for the first time demonstrate that TiPSCs can effectively differentiate into functionally active NK cells without M210-B4 and AFT-024 xenogeneic stroma cells. Immunofluorescence and flow cytometry analysis showed that EB-derived cells can differentiate into a homogeneous population of NK cell expressing high levels of CD56, CD45 and CD16 specific markers. Moreover, these cells significantly express killing activation receptors such as NKp44 and NKp46. In the comparative analysis, we observed that NK cells derived using feeder-free culture system have more high killing activity against K-562 tumor cells, than NK cells derived by feeder-dependent method. Thus, we think that our obtained data will be useful for the development of large-scale production of NK cells for translation into cancer immunotherapy.

Keywords : induced pluripotent stem cells, NK cells, T cells, cell diffentiation, feeder cell-free culture system
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