EuroSciCon

15th Edition of EuroSciCon Conference on

Advanced Stem Cell & Regenerative Medicine

December 03-04, 2018
Valencia, Spain

J Stem Cell Biol Transplant 2018, Volume 2
DOI: 10.21767/2575-7725-C1-003

Harnessing PU.1 and GATA-1 axis for priming human CD34+ stem cells towards myeloid lineages

Madhuri Joshi and **Gurudutta Gangenahalli**
INMAS-DRDO, India

The active immunity in an immune compromised or radiation victim can be restored by generating functionally competent immune cells. Transcription factor like PU.1 plays a critical role in the differentiation of hematopoietic stem cells (HSCs) into immune cells. Another transcription factor GATA-1 (43 kDa) interacts with PU.1, which promotes differentiation of HSCs into erythroid lineages by blocking the binding of its coactivator c-Jun with β3/β4 region of PU.1. We have established an antagonizing mutation (Y244D) in β3/β4 domain by site-directed mutagenesis of PU.1, anticipating the enhancement of myelopoiesis if introduced into cells. We further assessed if it can really antagonize GATA-1 and promote myelopoiesis in cells upon transfection of native and mutant PU.1 protein formulated into nanoparticle structure. Approximately 30% of human bone-marrow CD34+ stem cells were transformed into myeloid lineage by using these NPs loaded with PLGA in vitro. In vivo studies by infusing primed CD34+ with these NPs and along with cytokines were conducted in irradiated nude mice. Results demonstrated higher survival rate (50-75%) in mice compared to control mice with a reasonable number of macrophages (43.11%) and neutrophils (50.44%) being observed on the 21st day. Further high-throughput microarray analysis in CD34+ cells whose selective differentiation was induced by PU.1 (Y244D) mutant transfection was performed to explore the myeloid specific gene-cluster responsible for myeloid development. Gene expression analysis demonstrated that a ≥2.5 fold change were observed in several genes like PRTN3, TLR4, EPAS1, FCER1A, NOD2, CBL, SMAD4, ANO6, TFRC, IL1R1 etc. Studies on establishing the role/mechanistic basis of these genes are presently under progress.

gugdutta@rediffmail.com