Efficient hematopoietic differentiation of human embryonic stem cells on stromal cells derived from hematopoietic niches.

Abstract:
Hematopoietic stem cells derived from human embryonic stem cells (hESCs) could provide a therapeutic alternative to bone marrow transplants, but the efficiency of currently available derivation protocols is low. In this study, we investigated whether coculture with monolayers of cells derived from mouse AGM and fetal liver, or with stromal cell lines derived from these tissues, can enhance hESC hematopoietic differentiation. We found that under such conditions hESC-derived differentiating cells formed early hematopoietic progenitors, with a peak at day 18-21 of differentiation that corresponded to the highest CD34 expression. These hESC-derived hematopoietic cells were capable of primary and secondary hematopoietic engraftment into immunocompromised mice at substantially higher levels than described previously. Transcriptional and functional analysis identified TGF-beta1 and TGF-beta3 as positive enhancers of hESC hematopoietic differentiation that can further stimulate this process when added to the culture. Overall, our findings represent significant progress toward the goal of deriving functional hematopoietic stem cells from hESCs.