

DERIVATION OF HEPATOCYTES AND HEMATOPOIETIC PROGENITORS FROM HUMAN EMBRYONIC STEM CELLS

View U.S. Patent Application Publication No. US-2023-0113074 in PDF format.

WARF: P210190US02

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The Invention

The inventors have developed a novel system for co-differentiation of hepatocytes and hematopoietic progenitors from human embryonic stem cells (ES cells) that mimics a late fetal liver undergoing hematopoiesis. Small hepatic progenitor cells (SHPCs) derived from these hepatocytes have shown mature metabolic functions as well as engraftment in immunodeficient mice. The differentiated hematopoietic precursors express mature markers that show promise for engraftment (study in progress).

The inventors found that differentiation of ES cells in co-culture with mouse embryonic fibroblasts (MEFs) under specific conditions (e.g., fresh MEFs, fresh media, low confluency) gives rise to both hepatic and hematopoietic lineages:

- 1) Hepatocytes generated in this system display late fetal markers (both albumin and alpha-fetoprotein, AFP) and give rise to mature and engraftable small hepatic progenitor cells (SHPCs, which express albumin but not AFP). To date, such SHPCs have been derived only from primary human hepatocytes (PHHs). The inventors have previously shown that such SHPCs express high levels of mature hepatic genes, perform xenobiotic metabolism at rates equal to primary human hepatocytes, and support engraftment in immunodeficient mice (P180325).
- 2) In this system, the hematopoietic progenitor cells (HPCs) arise in two waves reminiscent of early and definitive hematopoiesis that occurs in vivo; these cells display typical HPC morphology and express the mature marker CD45 (and not the early marker CD43).

Additional Information

For More Information About the Inventors

• James Thomson

Tech Fields

- Pluripotent Stem Cells: Culture
- Pluripotent Stem Cells: Differentiation
- Therapeutics & Vaccines : Biologics

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