Identification of a Factor that Promotes Human Hematopoietic Stem Cell Self-Renewal

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SUMMARY

The Mikkola group at UCLA has discovered a novel regulator of hematopoietic stem cell self-renewal. The overexpression of this regulator increases the yield of ex vivo stem cell expansion and could thereby improve the efficiency of stem cell therapies.

BACKGROUND

Blood cells are responsible for the maintenance and immune protection of nearly every cell type in the body. It is therefore unsurprising that this relentless work would require blood cells to self-renew. This self-renewal process begins with hematopoietic stem cells (HSCs). HSCs are responsible for the constant renewal of blood cells – reaching production values of billions of new cells each day. Basic research in the 1950's looked to use this process of constant renewal to treat diseases.

Following initial success in disease states, HSC therapy worked its way into therapies for: cancer, immunodeficiencies, hematological diseases, and genetic disorders. One key issue in the use of HSCs for these therapies is the difficulty to expand cultures ex-vivo. Therefore, the identification of a method that would increase the number of transplantable stem cells obtained during the process of ex-vivo expansion, could propel the success of HSC cell-based therapy in several disease models.

INNOVATION

Dr. Mikkola at UCLA has discovered a novel regulator of HSC differentiation that is specifically expressed on human HSCs, but not expressed on human stem/progenitor cells (HSPCs). When the marker is upregulated during ex-vivo expansion, the observed engraftment of these HSCs into immune-compromised mice is remarkably heightened. Furthermore, the overexpression of this factor did not reveal conferment of renewal properties to non-self-renewing hematopoietic progenitors. This observation suggests that overexpression of the factor does not reprogram the progenitors of HSCs or leukemic stem cells but instead enhances the self-renewal of undifferentiated HSPCs. Therefore, the discovery of this novel factor may be used to more efficiently expand human HSCs ex-vivo, improving HSC transplantation and its use for various disease models.

APPLICATIONS

- Maintain HSC self-renewal
- Improve the population of transplantable HSCs during ex vivo expansion
- Prolong the maintenance of immunophenotypic HSPC populations

ADVANTAGES

- Increased efficiency and safety of HSC transplantation
- Does not give self-renewing properties to non-self-renewing progenitor cells
- May provide better in vitro models for PSC-derived hematopoiesis
- Improved expansion capacity could enable "disease-in-a-dish" studies for hematological diseases using patient specific iPSC or other pluripotent stem cells

STATE OF DEVELOPMENT

CONTACT

UCLA Technology Development Group
ncd@tdg.ucla.edu
tel: 310.794.0558.

INVENTORS

- Mikkola, Hanna KA.

OTHER INFORMATION

KEYWORDS

hematopoietic stem cells, HSC, HSPC, self-renewal, cell-based therapy, gene therapies, ex vivo stem cell expansion

CATEGORIZED AS

- **Medical**
  - Disease: Blood and Lymphatic System
  - Disease: Genetic Diseases and Dysmorphic Syndromes
  - Gene Therapy
  - Research Tools
  - Stem Cell
  - Therapeutics
- **Research Tools**
  - Other

RELATED CASES

2016-990-0

The invention has been tested during in-vitro studies, showing: that decreased expression of the novel factor leads to the loss of the proliferative capacity of HSCs, overexpression of the factor led to enhanced immunophenotypic HSPCs. Studies in-vivo in mouse models revealed that downregulation of the factor led to impaired HSC engraftment, while upregulation of the factor led to increased engraftment.

RELATED MATERIALS

- Magnusson, M. et al. Expansion on Stromal Cells Preserves the Undifferentiated State of Human Hematopoietic Stem Cells Despite Compromised Reconstitution Ability. PLOS ONE 8, e53912 (2013).
- Nsair, A. et al. Characterization and Therapeutic Potential of Induced Pluripotent Stem Cell-Derived Cardiovascular Progenitor Cells. PLOS ONE 7, e45603 (2012).

PATENT STATUS

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UCLA Technology Development Group

10889 Wilshire Blvd., Suite 920,Los Angeles,CA 90095

https://tdg.ucla.edu

Tel: 310.794.0558 | Fax: 310.794.0638 | ncd@tdg.ucla.edu