Enhanced Expansion of Hematopoietic Stem Cells for Autologous Stem Cell Therapy

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Background & Unmet Need

- Hematopoietic stem cells (HSCs) play an essential role in promoting the lifelong production of mature blood cell lineages
- Stem cell transplantation (SCT) using donor-derived HSCs is an effective therapy to treat multiple hematological malignancies and cancers, including leukemia and myeloma
- However, current SCT methods suffer from limitations in effectively processing an adequate number of HSCs
- Additionally, present technologies are incapable of maintaining or expanding human HSCs ex vivo
- **Unmet Need**: There is a need for methods that effectively expand HSCs for use in SCT therapies

Technology Overview

- **The Technology**: Cornell inventors have identified several methods that allow for robust ex vivo expansion of HSCs for research and clinical use
- **PoC Data**: Human-derived HSCs cultured under hypoxic conditions (1% O₂) demonstrated increased expression of CD34+ cells, a phosphoglycoprotein which is used clinically to quantify HSCs levels (see Figure 1A)
- Co-culturing HSCs with endothelial feeder cells (ECs) also increased CD34+ expression in addition to similar markers of HSC levels (CD45, iHSC), see Figure 1B
- Treating cell cultures with N-acetyl cysteine (NAC), an antioxidant that reduces cellular damage from reactive oxygen species, likewise enhances expression of markers of HSC availability (see Figure 1C)

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Patents:
US Application Filed
EP Application Filed

Publications:

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**Technology Applications**
- Described methods effectively enhance HSC expansion and may increase efficacy of SCT therapies.
- Methods may also be used to expand HSCs for research purposes.
- Ability to maintain viable HSCs ex vivo affords ability to modify the cells (e.g., genetic manipulations).

**Supporting Data / Figures**

**Figure 1**: *Ex vivo* methods to expand HSCs.  
A. In HSCs cultured under conditions with varying oxygen levels, lower oxygen levels were associated with increased CD34+.  
B. Co-culturing HSCs with endothelial feeder cells (ECs) enhanced expression of HSC markers (CD45, CD34, iHSC).  
C. Treatment of cells with the antioxidant N-acetyl cysteine (NAC) also enhanced expression of HSC availability markers (CD45, CD34, CD90).

**Technology Advantages**
- Multiple methods to expand HSCs may be used in isolation or in synchrony to enhance HSC expansion effects.
- Described culturing conditions are easy to implement and produce robust effects on HSC expansion.

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**Figure 2:** Schematic overview of the technology and associated clinical applications.

Expand repopulating human adult HSCs stem for clinical application

Enable autologous hematopoietic stem cell transplantation (HSCT) using genome-modified adult HSCs

- Gene-Modified Graft
- Autologous HSCT

Need to Fix a High-Enough Proportion of Adult HSCs to Cure Phenotype

Need Great-Enough Number of Adult HSPCs to Make Auto HSCT Safe

- Expand HSPCs when harvest is inadequate (SCD)
- Maintain HSCs during and after transduction
- Enable in vitro purging (selection)?
- Improve Transduction of HSCs?

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