Docket #: S22-269

Inducing TCL1A Expression to Increase Proliferation and Prolong Stemness of Hematopoietic Stem Cells

One of the main shortcomings of the clinical use of Hematopoietic Stem Cells (HSCs) is the limited number of cells that can be safely harvested from a patient. Inventors at Stanford have achieved over-expression of TCL1A in HSCs,thereby, increasing proliferation of HSCs, increasing their self-renewing capacity, and improving their resiliency.

Additional shortcomings of stem cell transplantation include, limited availability of suitable donor tissue, increased risk of lethal infections during the extended engraftment period, intensive caustic chemotherapy to provide a niche for donor cells and stressful genetic editing of blood cells. Current solutions including using multiple units of donor tissue and high dose antibiotics, supportive care and using high cell numbers to compensate for expected loss are not ideal. The ideal solution would be effective ex vivo expansion of HSCs, faster engraftment kinetics, more competitive HSCs that don't require niche to be cleared and more resilient HSCs that can endure genetic editing. Stanford researchers have identified one such ideal solution via endogenous temporary expression of TCL1A, which plays a role in cell survival and proliferation. This discovery can be put to therapeutic use by designing TCL1A mRNA or protein paired with appropriate delivery methods to temporarily drive TCL1A expression in HSCs.

Stage of Development
In vivo: Transplant of TCL1A overexpressing HSCs dramatically improved survival of mice following a lethal total body radiation conditioning regime

Applications

- HSC transplantation
- HSC gene editing

Advantages

- Novel method
- Expansion of HSCs ex vivo or in vivo
- Tunable temporal expression of TCL1A
- Expedite engraftment of autologous and allogeneic transplants
- Reduce chemotherapy required for successful engraftment
- Expand and expedite engraftment of edited cells
- Improve HSC survival during genetic editing process
- TCL1A may also have regenerative effects in other tissues stem cell types as well

Publications

- Weinstock, J. S., Gopakumar, J., et al. (2021). "Clonal hematopoiesis is driven by aberrant activation of TCL1A." bioRxiv, 2021-12

Patents

- Published Application: WO2024039600

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