Methods of Producing Thymic Emigrants from Induced Pluripotent Stem Cells

Summary (1024-character limit)

Pluripotent stem cells are a promising source of T cells for a variety of clinical applications. However, current in vitro methods of T cell differentiation result in the generation of cells with aberrant phenotypes. Researchers at the National Cancer Institute (NCI) have now developed methodology for generating induced pluripotent stem cell thymic emigrants (iTE). Antigen-specific CD8+ iTEs exhibited functional properties in vitro that were almost indistinguishable from natural naïve CD8+ T cells, including vigorous expansion and robust anti-tumor activity. iTEs recapitulated many of the transcriptional programs of naïve T cells in vivo and revealed a striking capacity for engraftment, memory formation, and efficient tumor destruction. The NCI seeks licensing and/or co-development research collaborations for this invention.

NIH Reference Number

E-250-2016

Product Type

- Therapeutics

Keywords

- Induced Pluripotent Stem Cells, iPSCs, T Cells, Thymic Environment, Differentiation, Research Material, Tool, Restifo

Collaboration Opportunity

This invention is available for licensing.

Contact

- John D. Hewes
  NCI - National Cancer Institute

  240-276-5515

  John.Hewes@nih.gov

Description of Technology

Hematopoietic and pluripotent stem cells can be differentiated into T cells with potential clinical utility. Current approaches for in vitro T cell production rely on Notch signaling and artificial mimicry of thymic selection. However, these approaches result in unconventional or phenotypically aberrant T cells; which may lead to unpredictable behavior in clinical use. Thus, there exists a need for improved methods of generating conventional T cells in vitro from stem cells.

Researchers at the National Cancer Institute (NCI) have developed a novel method for the in vitro differentiation of induced pluripotent stem cells (iPSCs) into induced pluripotent stem cell thymic emigrant (iTE) cells. Cells produced by this method are functionally equivalent to natural naïve CD8+ T cells. The approach utilizes improved fetal thymic organ culture methodology to mature progenitor cells into conventional T cells in the presence of extrinsic Notch signaling. Cell culture conditions further provide for positive and negative selection to ensure proper maturation. This method produces conventional T cells that are suitable for clinical applications such adoptive cell therapy.

The NCI, Surgery Branch, is seeking statements of capability or interest from parties interested in licensing or collaborative research to further develop, evaluate, or commercialize this method of generating naïve T cells from iPSCs.

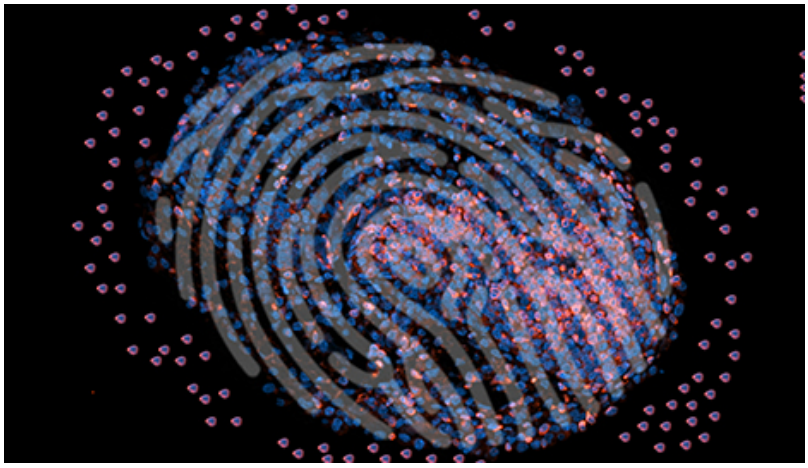

Image: A visual allegory of the generation of iPSC-derived thymic emigrants (in red).
Photo credit: Michael J. Kruhlak, Experimental Transplantation and Immunology Branch (ETIB)

CCR News: https://ccr.cancer.gov/news/article/stem-cell-technology-rejuvenates-can...

Potential Commercial Applications

- Applicable for the generation of minimally differentiated T-cells for cancer therapy and broad repertoires of T-cells for patients with lymphopenia

Competitive Advantages

- Long term development of this technology can be applied to a wide range of services in regenerative medicine and immunology
- Improved fetal thymic organ culture methodology using a hanging-drop system

Inventor(s)

Raul E Vizcardo (NCI), Nicholas D Klemen (NCI), Nicholas P Restifo (NCI)

Development Stage

- Pre-clinical (in vivo)

Publications

Vizcardo, R, et al. Generation of tumor antigen-specific iPSC-derived thymic emigrants using a 3D thymic culture system. [PMID 29562175]

Patent Status

- **U.S. Patent Filed:** U.S. Patent Application Number 16/468,890, Filed 12 Jun 2019
- **PCT:** PCT Application Number PCT/US2017/065986, Filed 13 Dec 2017

Related Technologies

- E-133-2017 - In vitro Generation of an Autologous Thymic Organoid from Human Pluripotent Stem Cells

Therapeutic Area

- Cancer/Neoplasm
- Infectious Diseases