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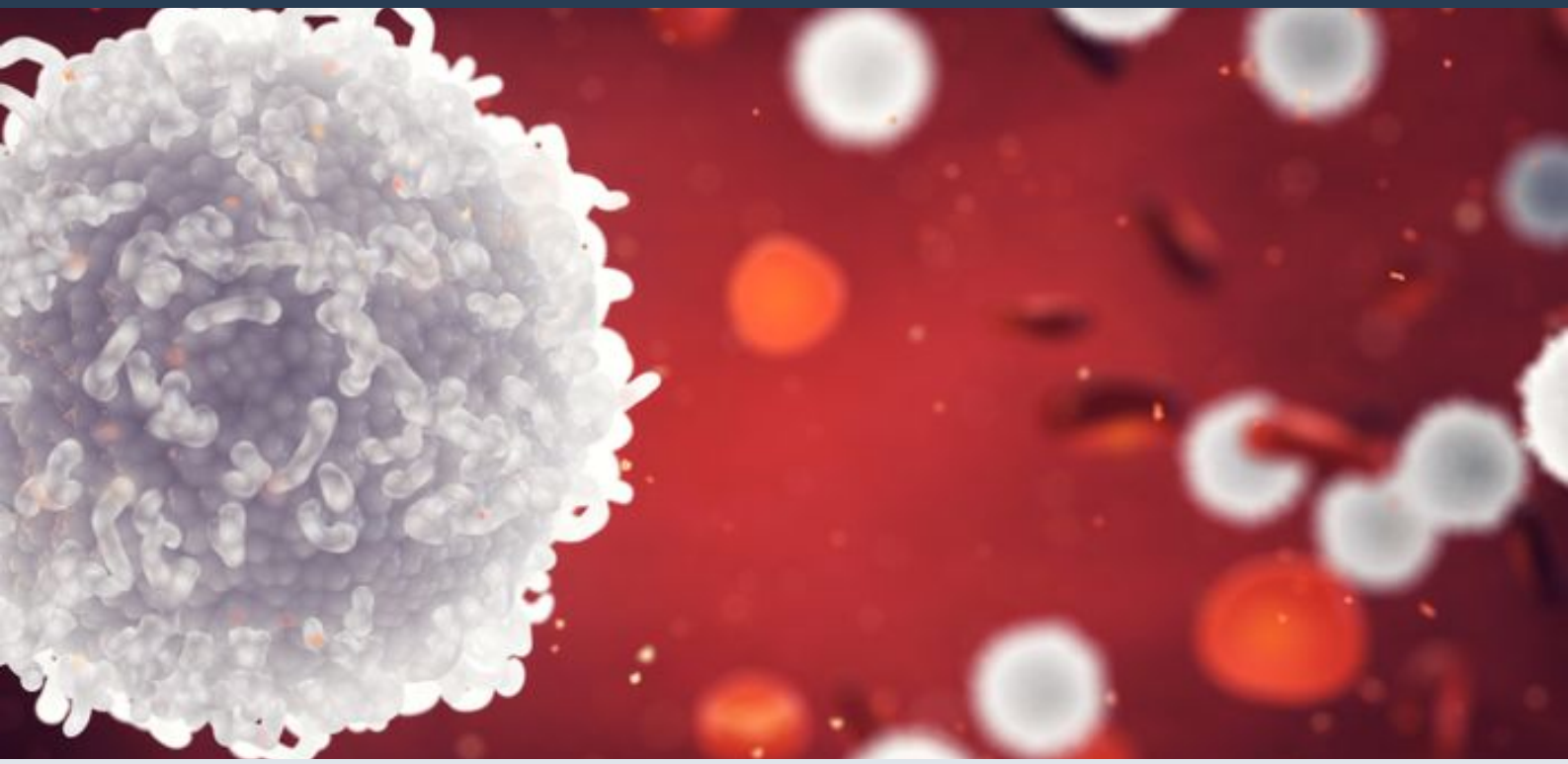
Inducible Transcription Factors (iTFs) for Large Scale ex vivo Production of Functional Human Blood Cells

Exploiting human transcription factors for rapid and large-scale ex vivo production of functional immune cells suitable for cell therapy

Reference: iTFs for Immune Cells



Source: https://stock.adobe.com/uk/297377241

Seeking

Development partner

About **LMU Munich**

Ludwig-Maximilians-Universität München is the University in the heart of Munich. LMU is recognized as one of Europe's premier academic and research institutions. The LMU Munich community is engaged in generating new knowledge for the benefit of society at large.

Background

Among stem cells, which originate and maintain human life, hematopoietic stem cells give rise to all functional blood cells, including immune cells, and therefore are used for transplantation in the treatment of cancers and immune system disorders. As long-term *ex vivo* expansion of hematopoietic stem and progenitor cells (HSPCs) seems to be unattainable, there is an urgent need to identify methods to accomplish efficient progenitor cell expansion. To achieve sufficient amounts of functional immune cells for therapeutic approaches, *ex vivo* expansion of human blood progenitor cells with the potential to differentiate into various immune cells, is a promising approach. The key hurdle is the rapid differentiation upon separating the cells from their hematopoietic niche.

Here LMU Munich researchers outline the concept of using leukemia-associated engineered inducible transcription factors (iTFs) conferring sustained and powerful self-renewal properties to human blood progenitors, able to differentiate into functional blood cells and therefore being of particular importance for patient-specific cell therapy approaches.

This technology represents an efficient and safe way to generate large amounts of immune cells for cell-based immuno-therapy approaches. Therefore, such iTFs will become valuable molecular tools for the large-scale generation of functional human blood/immune cells.

Tech Overview

The key point of this technology is the genetic manipulation of human hematopoietic stem cells to enable rapid and long-term expansion of progenitor cells with the ability to differentiate to functional immune cells. The inducible transcription factor (iTF) is stably expressed in HSPCs via retroviral transduction leading to a fast and long-term expansion of immature cells. As the proliferation of the cells is fully dependent on the activity of the transcription factor, even after two years, shutdown of the iTF set the stage for differentiation into immune cells using stimulating cytokines.

Key points:

- Single factor (gene) remarkable expansion, no additional mutations during extensive long-term culture of human blood progenitors
- Inducible expansion genes
- Stable, retroviral transduction into human CD34+ cells long-term expression
- Expansion gene can be easily turned off
- Differentiation towards functional blood cells
- Functional assays using differentiated cells
- Comparison with physiological immune cells

Further Details

- Graphical Abstract
- https://www.sciencedirect.com/science/article/pii/S1465324920300840

Stage of Development

Proof of Concept:

- iTF development
- Long-term expansion (>2 years)
- Functional immune cells: e.g. proof of macrophage functionality
- Gene expression profiling

Benefits

- Easy to generate humane immune cells
- Convenient genetic engineering (e.g. co-delivery of CAR constructs)
- Only a single gene is necessary for programming of blood stem cells
- No time-consuming reprogramming compared to iPS cells

Applications

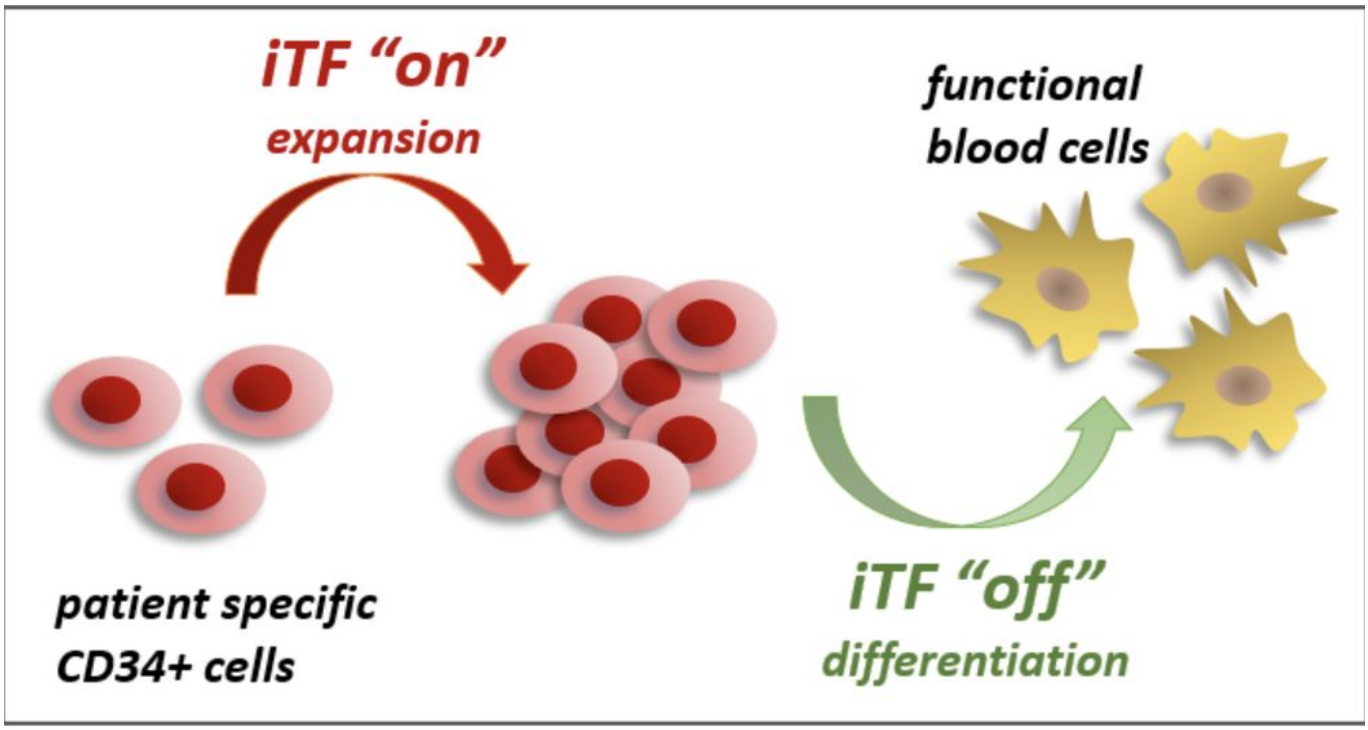
- Treatment of immune cell defects
- Production of designer immune cells, e.g. cancer-targeting macrophages (CAR macrophages) for leukemia and solid tumors
- Immune cells for research purposes (e.g. infectious biology)

Opportunity

Development partner and funding for methodical improvement and method/concept development.

Appendix 1

Graphical Abstract



For further information, please contact us.

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