Transient Modified-RNA Expression of Activation Factor Promotes Adult Hematopoietic Stem Cell Expansion

Lead Inventors:

**Tomer Itkin, Ph.D.**
Instructor of Biology in Medicine, Medicine, Weill Cornell Medical College

**Shahin Rafii, M.D.**
Professor of Medicine, Medicine, Weill Cornell Medical College
Arthur B. Belfer Professor in Genetic Medicine
Chief, Division of Regenerative Medicine
Director, Ansary Stem Cell Institute

Business Development Contact:
Dan-Oscar Antson
Technology Licensing Officer
(646) 962-7042
da429@cornell.edu
# Transient Modified-RNA Expression of Activation Factor Promotes Adult Hematopoietic Stem Cell Expansion

## Background & Unmet Need

- **Hematopoietic Stem Cell (HSC) transfer and transplantation** is a life-saving treatment for many diseases, including cancers and blood disorders.
- Human mobilized peripheral blood (mPB) is the most accessible source of Hematopoietic Stem and Progenitor Cells (HSPCs).
- However, there can be insufficient numbers of available transplantable mPB HSPCs following extraction or following ex-vivo genetic therapy.
- Moreover, mPB HSPCs are much less proliferative than HSPCs from other sources, such as cord blood, and are less likely to respond to current expansion protocols.
- **Unmet Need:** Activation methods for mPB-derived HSPC robust expansion for successful stem cell transplants resulting with full recovery and reconstitution of blood and immune systems.

## Technology Overview

- **The Technology:** A method for ex-vivo activation of HSPC expansion using a modified-RNA to overexpress a defined transcription factor.
- **The Discovery:** The inventors have discovered a master transcriptional regulator for HSPC activation, which can direct HSPC regenerative expansion from a quiescent non-cycling state.
- This activation factor mediates the crosstalk between HSPCs and their niche and sensitizes them to expansionary regenerative signals.
- Treatment with modified RNA to induce over-expression of this factor or downstream activation factors can prime HSPCs for robust expansion.
- **PoC Data:** Human adult mPB HSPCs treated with this modified-RNA had increased expansion and superior engraftment capacity in vivo matching that of neonatal cord blood-derived HSPCs.

## Inventors:
- Tomer Itkin
- Shahin Rafii
- Lior Zangi

## Patents:
- Provisional Filed

## Publications:
- N/A

## Biz Dev Contact:
- Dan-Oscar Antson
- (646) 962-7142
da429@cornell.edu

## Cornell Reference:
- D-10278
Transient Modified-RNA Expression of Activation Factor Promotes Adult Hematopoietic Stem Cell Expansion

### Technology Applications
- Ex-vivo, pre-transplantation expansion of adult bone marrow or peripheral blood mobilized HSPCs
- Use for patients with poorly-mobilizing mPBs (e.g. due to genetic factors, diabetes, immunotherapy, chemotherapy)
- Pre-engraftment expansion of HSCs following successful genetic therapy for gene replacement (e.g. beta-thalassemia)

### Technology Advantages
- Increased adult HSPC activation and expansion
- Expanded HSCs successfully engraft when transplanted displaying higher numbers of repopulating cells
- Transient expression using modified-RNA technology limits the risk of tumorigenesis or stem cell exhaustion associated with constitutive expression of activation factors

### Supporting Data / Figures

**Figure 1**: Summary diagram of HSPC expansion and transplantation from mobilized peripheral blood.

<table>
<thead>
<tr>
<th>Sorted mPB CD34+ cells</th>
<th>Mod-RNA Transduction</th>
<th>Expansion</th>
<th>Transplant into NSG mice</th>
</tr>
</thead>
</table>

**Inventors:**
- Tomer Itkin
- Shahin Rafii
- Lior Zangi

**Patents:**
- Provisional Filed

**Publications:**
- N/A

**Biz Dev Contact:**
- Dan-Oscar Antson
  - (646) 962-7142
daa429@cornell.edu

**Cornell Reference:**
- D-10278
Figure 2: **Left:** Adult mPB HSPCs treated with mod-RNA demonstrate similar expansion capacity as cord blood-derived HSPCs. **Right:** Chimerism is higher in mice with transplanted mPB HSPCs treated with mod-RNA, indicating higher engraftment levels.