### Ex Vivo Gene Editing of Human Hematopoietic Stem Cells for the Treatment of X-Linked Hyper-IgM Syndrome

#### Grant Award Details

**Grant Type:** Therapeutic Translational Research Projects  
**Grant Number:** TRAN1-11536  
**Project Objective:** To conduct a pre-IND meeting and prepare protocol for CRISPR/Cas9 gene edited autologous HSC therapy for X-linked Hyper IgM Syndrome.

<table>
<thead>
<tr>
<th>Investigator</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Name:</strong></td>
<td>Caroline Kuo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Institution:</strong></td>
<td>University of California, Los Angeles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Type:</strong></td>
<td>PI</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Disease Focus:** Blood Disorders, Hyper IgM Syndrome, Immune Disease  
**Human Stem Cell Use:** Adult Stem Cell  
**Award Value:** $4,896,628  
**Status:** Active

#### Grant Application Details

**Application Title:** Ex Vivo Gene Editing of Human Hematopoietic Stem Cells for the Treatment of X-Linked Hyper-IgM Syndrome
Public Abstract: **Translational Candidate**

Human hematopoietic stem cells that have been gene-corrected at the CD40L gene to treat patients with X-Linked Hyper-IgM Syndrome

**Area of Impact**

These studies will bring stem cell gene therapy for XHIM closer to the clinic especially those without an HLA match or infections too severe for HSCT.

**Mechanism of Action**

The CRISPR/Cas9 platform allows site-specific integration of a corrective copy of the CD40L gene at its normal location, maintaining expression of the corrective DNA under control of natural regulatory elements. Transplantation of gene-corrected hematopoietic stem cells, which are self-renewing and long-lived, produces all blood lineages, including T lymphocytes with restored CD40L expression that can stimulate B cells to produce class-switched immunoglobulin.

**Unmet Medical Need**

There is no curative treatment for XHIM patients without a bone marrow match or with severe infections. Gene corrected HSC can cure XHIM and provides a therapeutic option for these patients. This proposal will advance the field of stem cell gene therapy and treatment of primary immunodeficiencies.

**Project Objective**

Pre-IND meeting

**Major Proposed Activities**

- Characterize clinical grade critical reagents in healthy and XHIM hematopoietic stem cells. Perform clinical scale run and pilot toxicology study.
- Assess off-target insertions and deletions caused by CRISPR/Cas9 in additional cell lines and in primary hematopoietic stem cells.
- Prepare clinical protocol, investigator’s brochure, consent forms, and Pre-IND package. Complete Pre-IND meeting with the FDA.

**Statement of Benefit to California:**

Safe, definitive therapies for XHIM represent an unmet medical need. Allogeneic stem cell transplant is frequently complicated by graft-versus-host disease and worsening of pre-existing infections. Successful demonstration that stem cell gene therapy can safely and effectively cure XHIM will shift the paradigm by which patients will be treated, led by California’s position as a leader in the field of gene therapy. This will result in improved patient care in the state and around the world.

**Source URL:** https://www.cirm.ca.gov/our-progress/awards/ex-vivo-gene-editing-human-hematopoietic-stem-cells-treatment-x-linked-hyper-igm