



UNIVERSITY of CALIFORNIA, SAN DIEGO
SCHOOL OF MEDICINE

HOW RARE DISEASE RESEARCH IS TRANSFORMING MEDICINE THROUGH GENE THERAPY

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE BOARD MEETING

SEPTEMBER 24, 2026

Stephanie Cherqui, Ph.D

Professor, Department of Pediatrics

Director of UCSD the Gene Therapy Initiative

Ben and Wanda Hildyard Chair for
Mitochondrial and Metabolic Diseases

DISCLOSURES

PROFESSIONAL ROLES AND AFFILIATIONS

- Chair, Scientific Review Board and Trustee, Cystinosis Research Foundation
- Cofounder, Shareholder, Board Member, and Scientific Board Member, Papillon Therapeutics Inc.



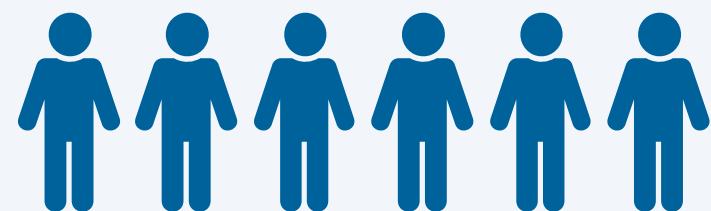
the RARE DISEASE PARADOX

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 While these diseases are "rare," **the collective burden is massive** and the unmet need is a global crisis!

LET'S TALK NUMBERS

In the United States, it is a **rare disease** if it affects:



**<200,000 people in
the United States**



>7,000

Number of rare
diseases



350-400 Million

Estimated people
affected worldwide



Less than 10%

Have an approved
therapy available



50%

Affect children



"Every rare disease is a small stream, but collectively they become a force too large to ignore."

what many

RARE DISEASES HAVE IN COMMON

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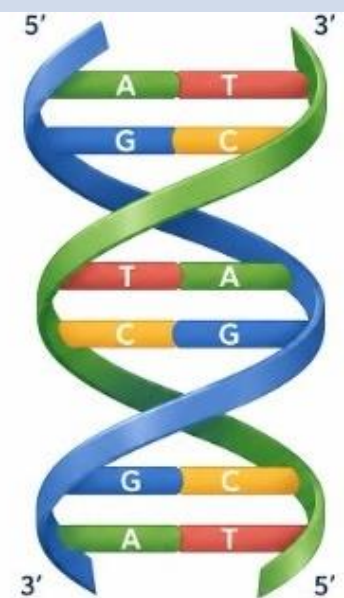
80%

Of rare diseases have a genetic origin caused by errors in our DNA



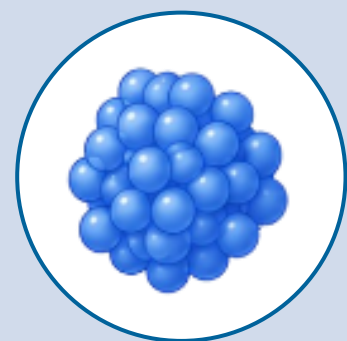
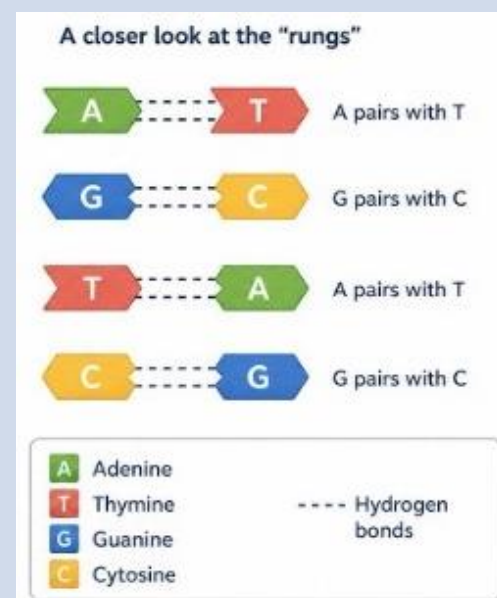
GENE THERAPY

is how we re-write the code to correct errors, enabling cells to function properly & treating the disease



DNA

contains the instructions that tell cells how to build and maintain the body.



PROTEINS

carry out the instructions in DNA to build structures, send signals, and perform essential functions.

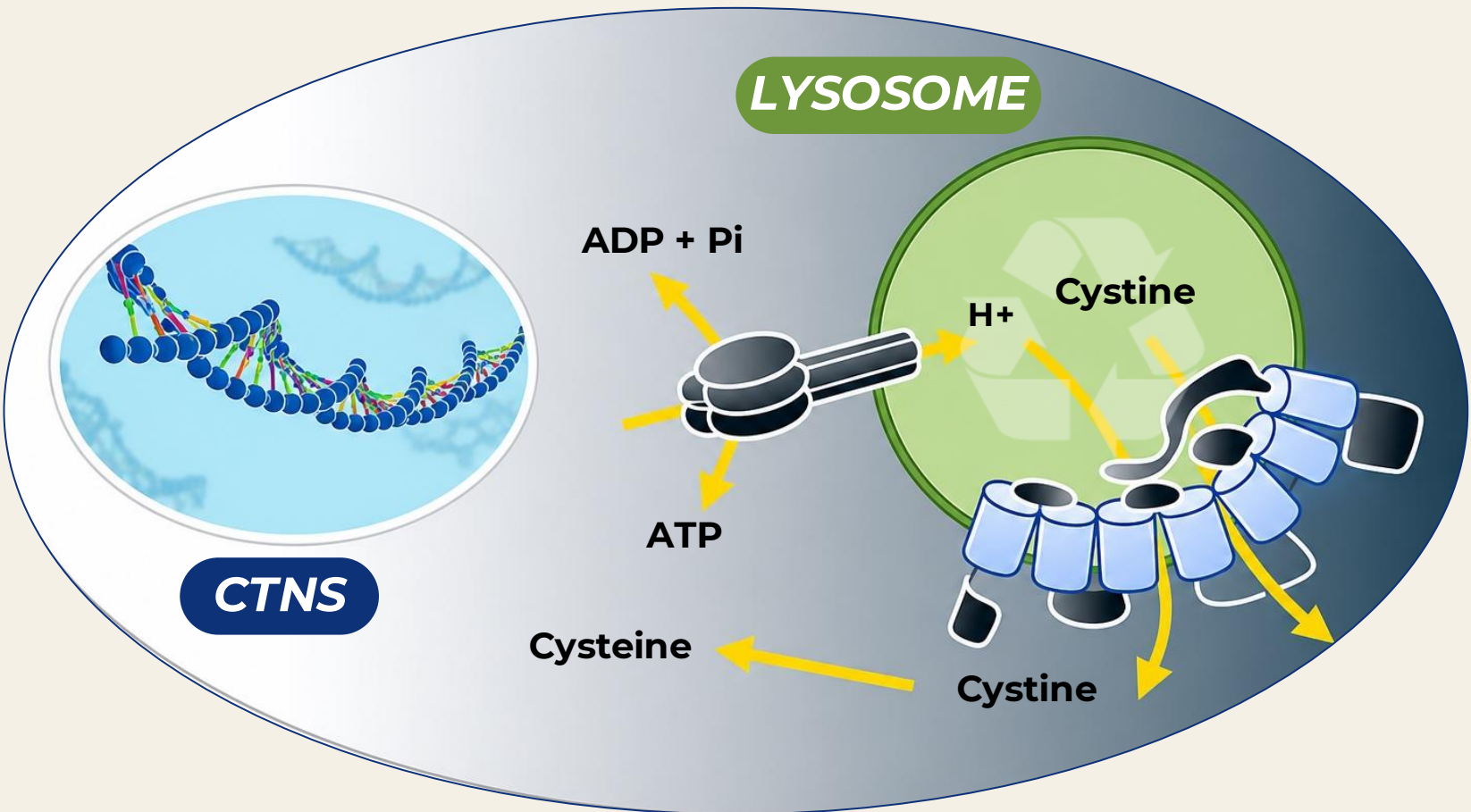
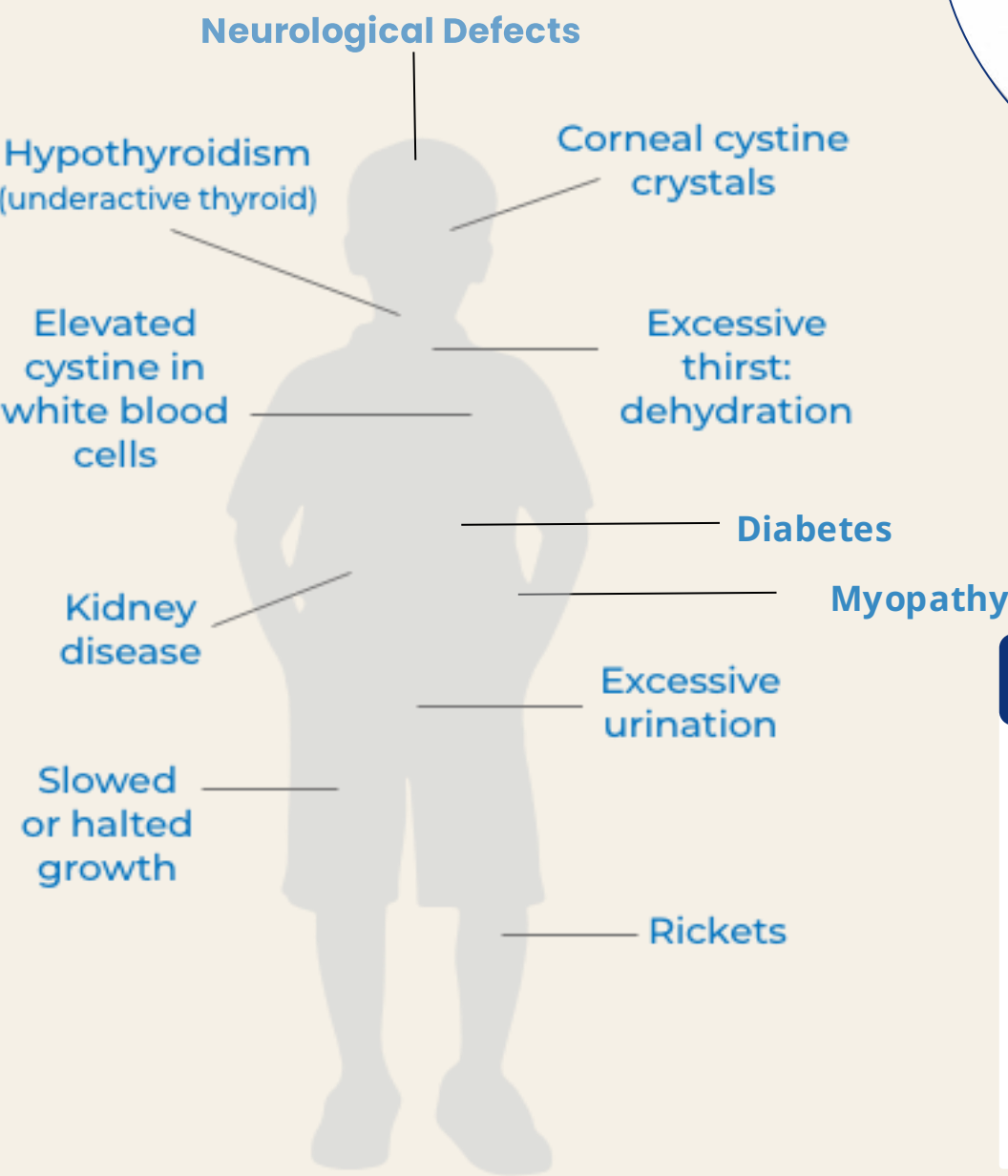
KEY ADVANTAGES

- **PRECISION:** Targets the root genetic cause
- **LONGEVITY:** Potential for one-time or durable benefit
- **TRANSFORMATIVE:** Superior outcomes relative to conventional drugs

Genetic Cause of CYSTINOSIS

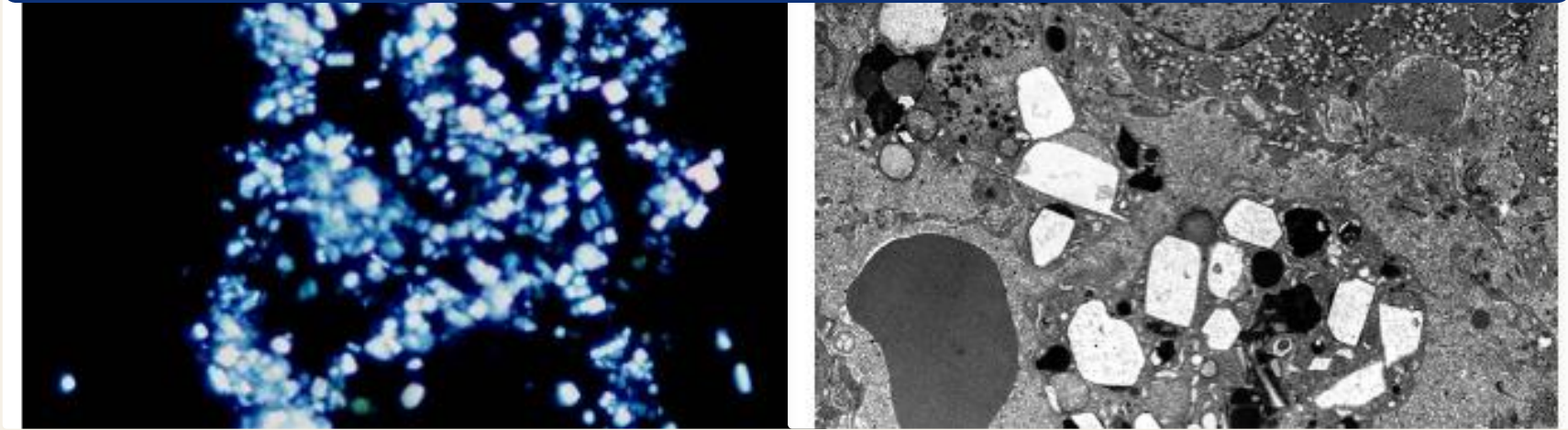
Rare metabolic disease

**BODY SYSTEMS AFFECTED BY
CYSTINOSIS**



! IN DISEASE CELLS CYSTINE GETS TRAPPED INSIDE THE LYSOZOME.

Cystine accumulation within lysosomes in all cells of the body

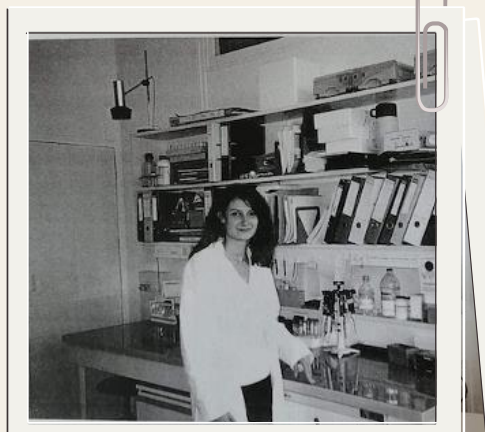


CTNS

The gene that codes for Cytsinosin. A defective CTNS gene lead to the disease.

CYSTINOSIN

A protein that transports cystine from cells and prevents harmful buildup.



Dr. Stephanie Cherqui as a Graduate Student
in Dr. Corinne Antignac's Lab

THE GENE THERAPY DILEMMA

The questions that started it all...



Which vehicle can deliver a working version of CTNS to ALL CELL TYPES where it is expressed?



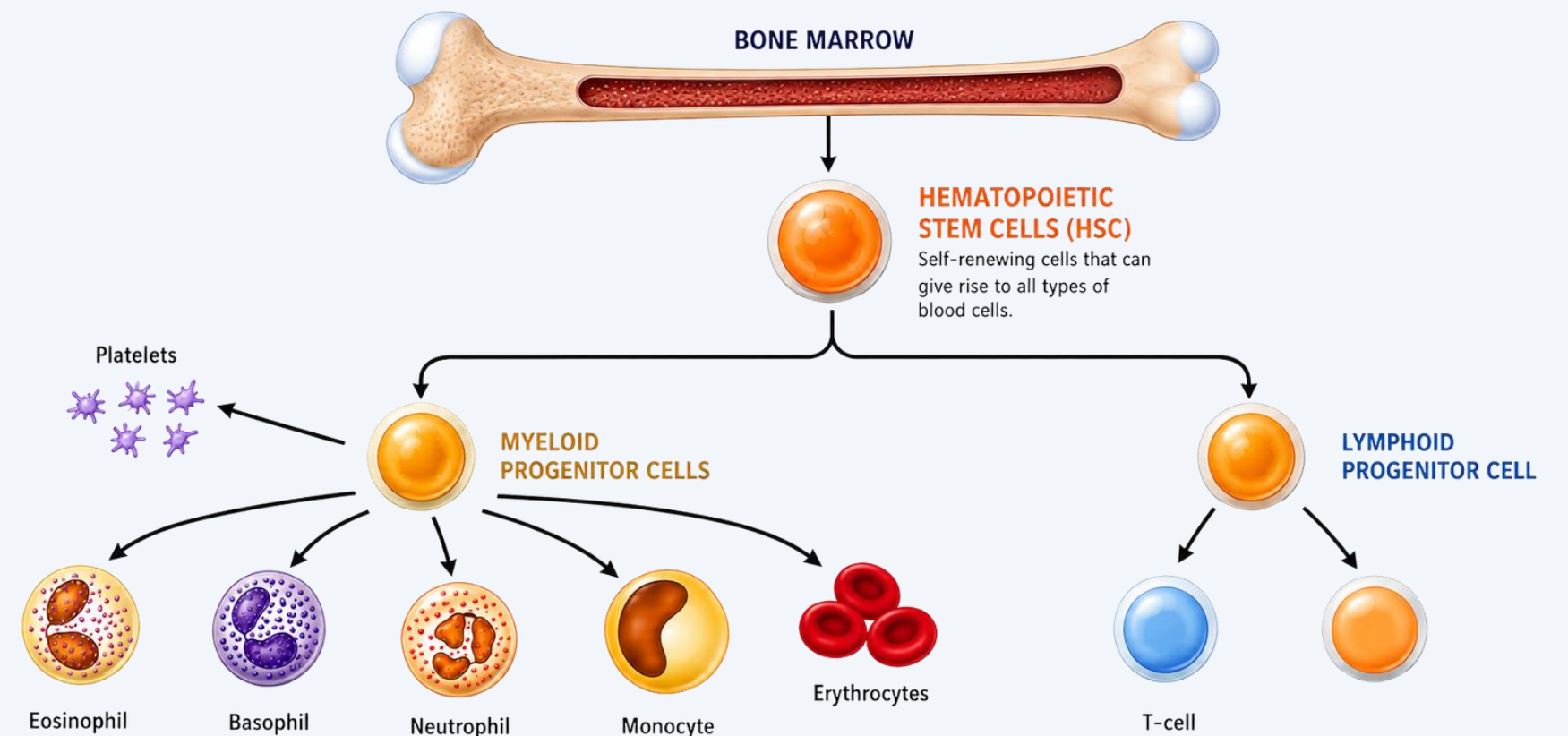
How can the healthy version of the Cystinosis protein reach the cells that need rescuing?



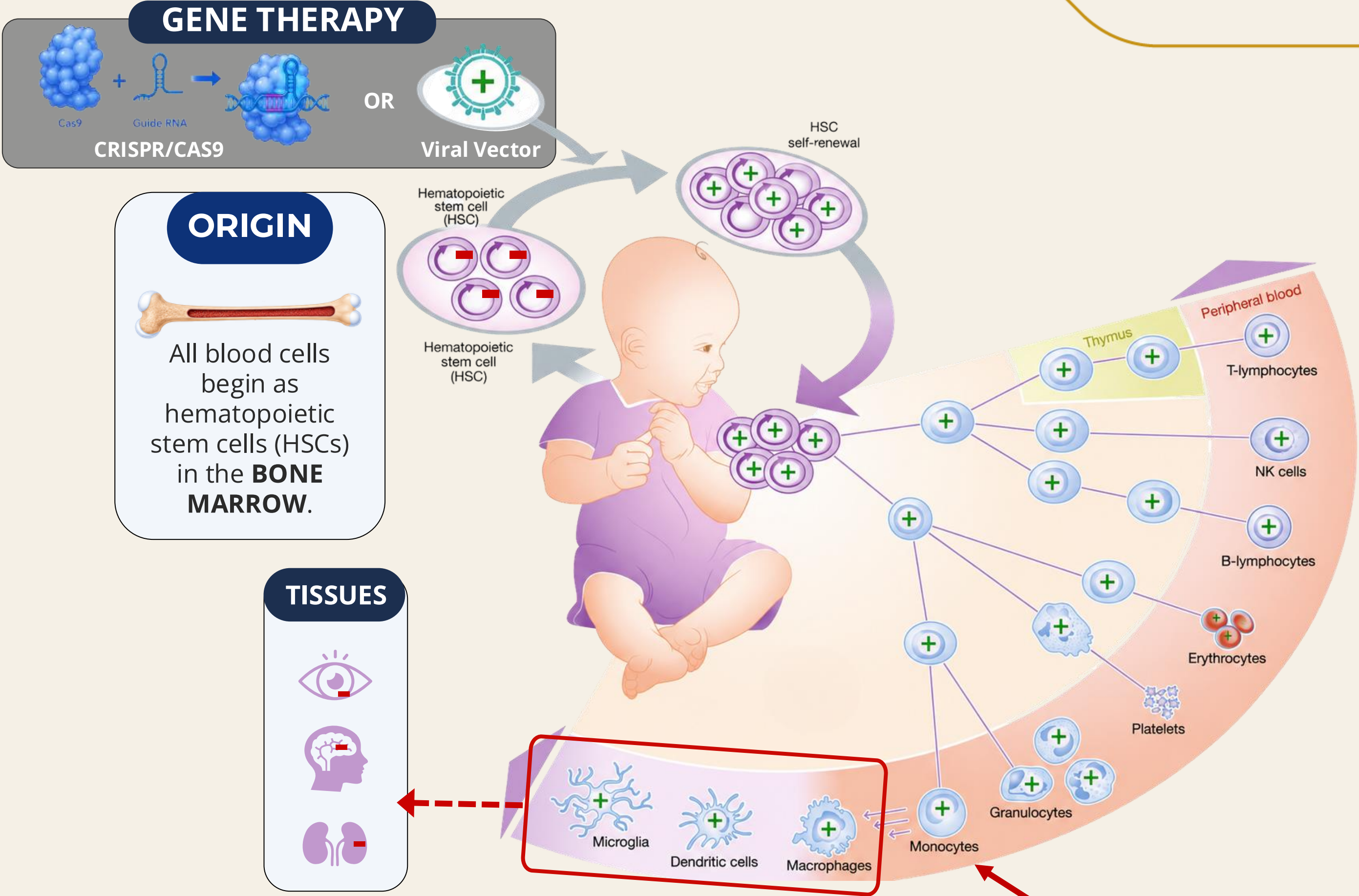
Is it possible to remove the accumulated cystine from sick cells?

HEMATOPOIETIC STEM CELLS (HSC)

Special stem cells found in the **bone marrow** that make all the different types of blood and immune cells your body needs throughout your life.



HEMATOPOIETIC STEM CELLS & Gene Therapy

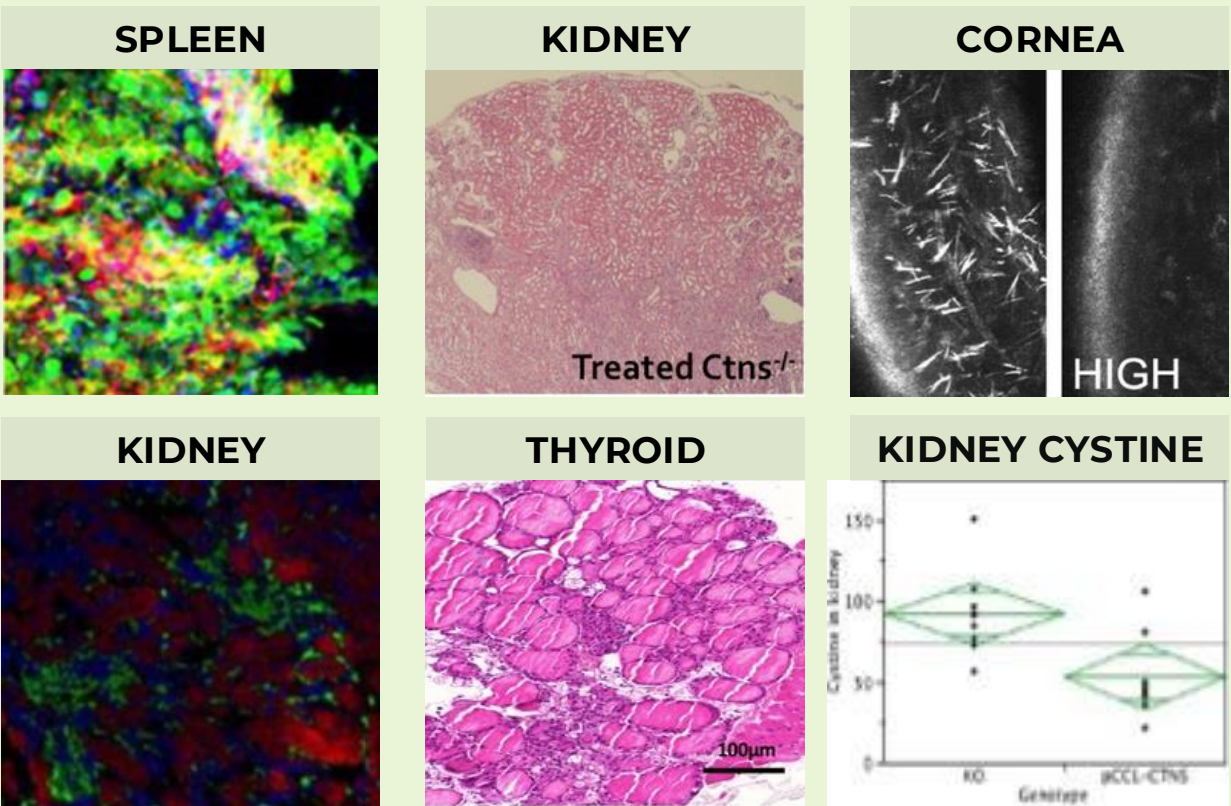
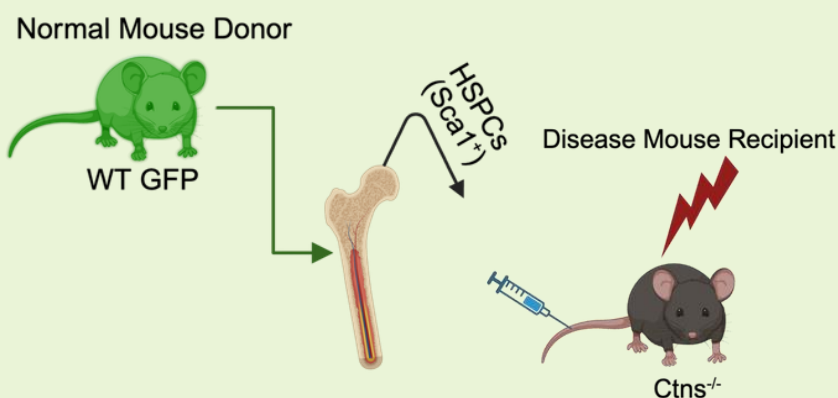


PRE-CLINICAL STUDIES

to

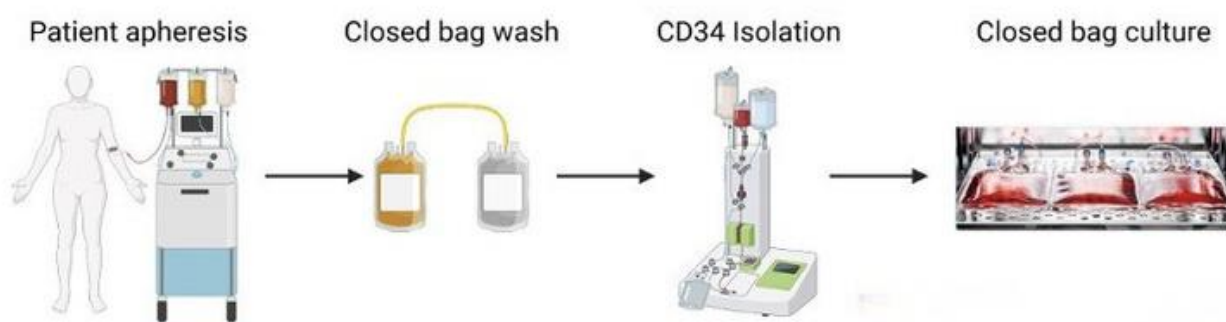
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Proof of Concept

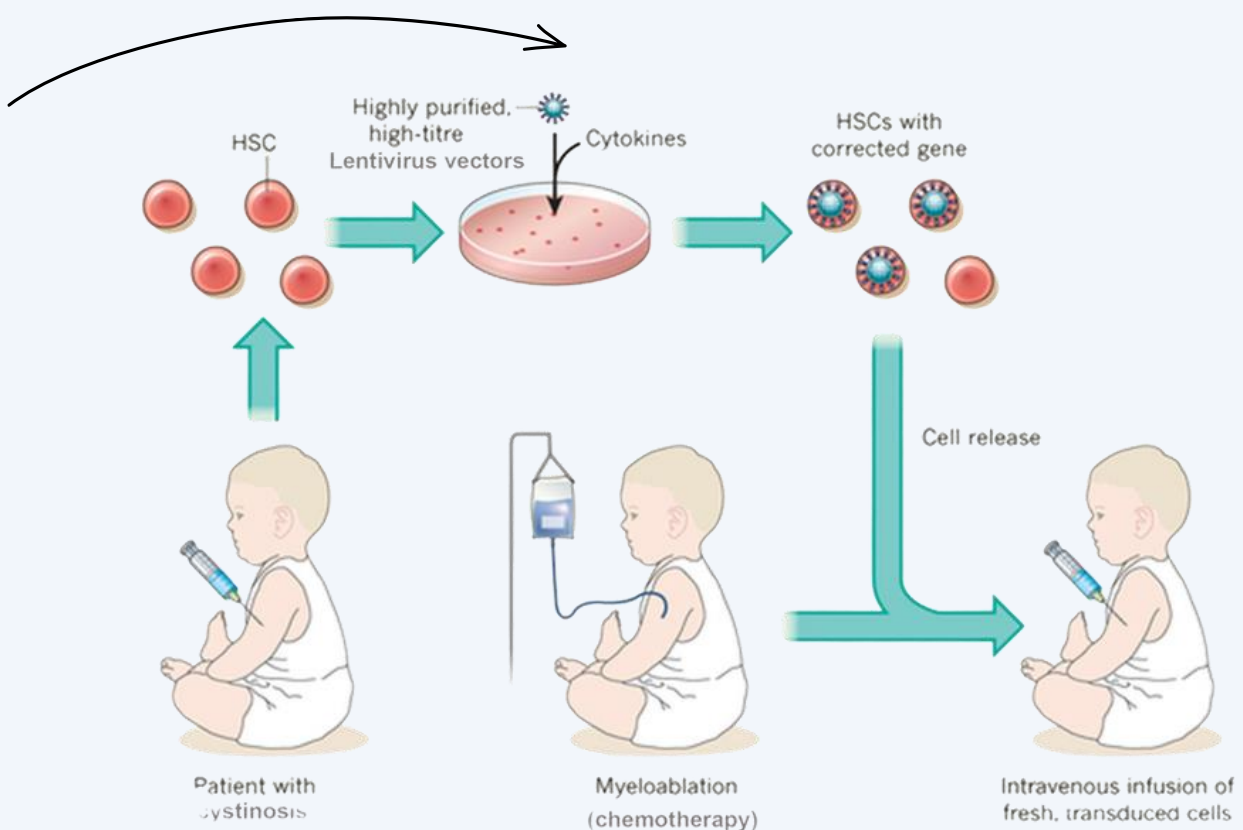
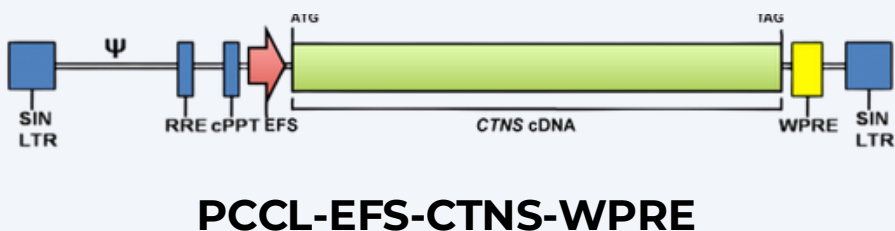


TRANSLATION

Manufacturing Development



Lentivirus vector (safe version of HIV)



Interaction with FDA



Investigational
New Drug
approved



PHASE 1/2 AUTOLOGOUS HEMATOPOIETIC STEM CELL GENE THERAPY CLINICAL TRIAL FOR CYSTINOSIS

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CIRM CLIN2 grant
CALIFORNIA INSTITUTE FOR
REGENERATIVE MEDICINE

ClinicalTrials.gov Identifier # NCT03897361

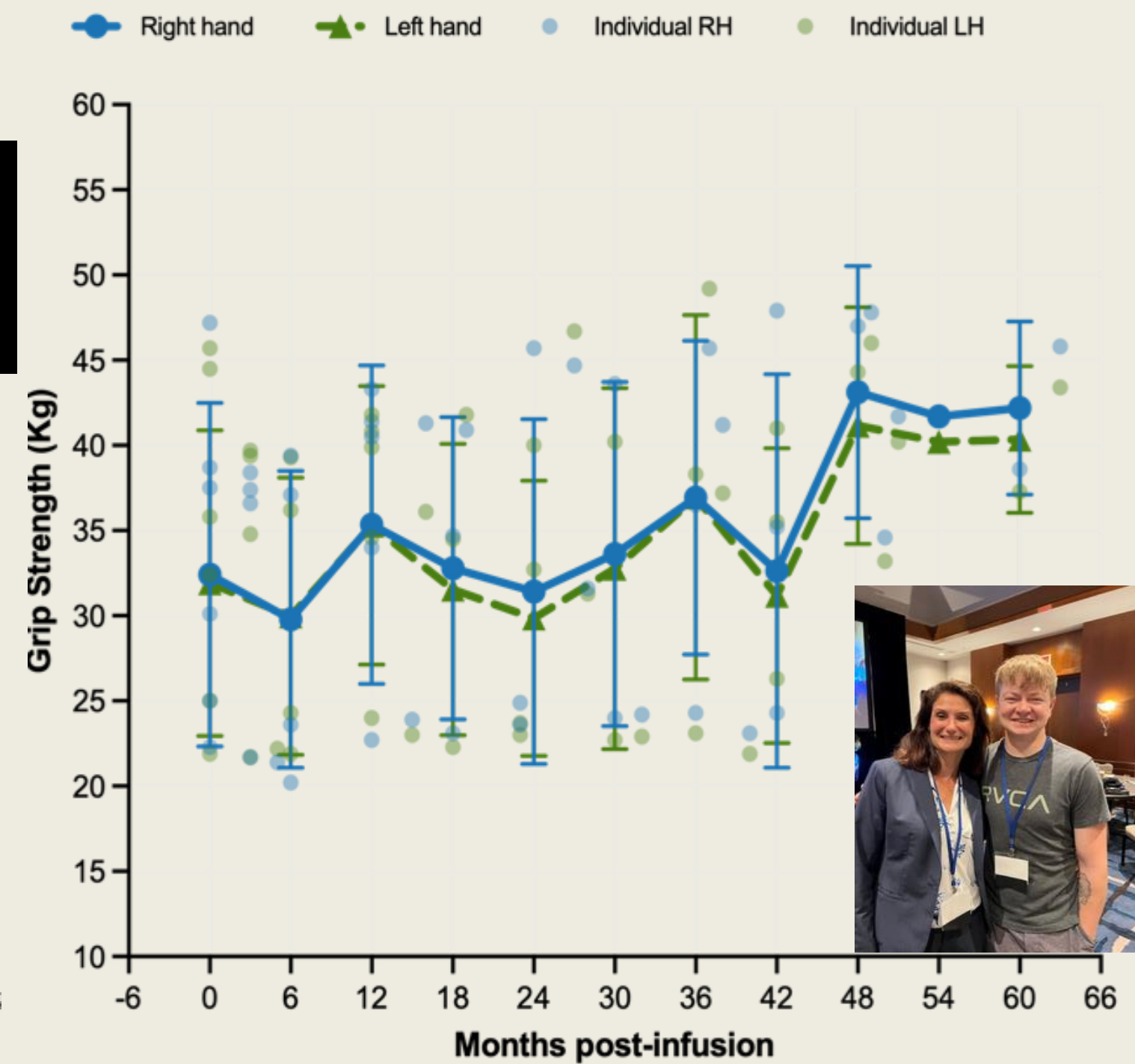
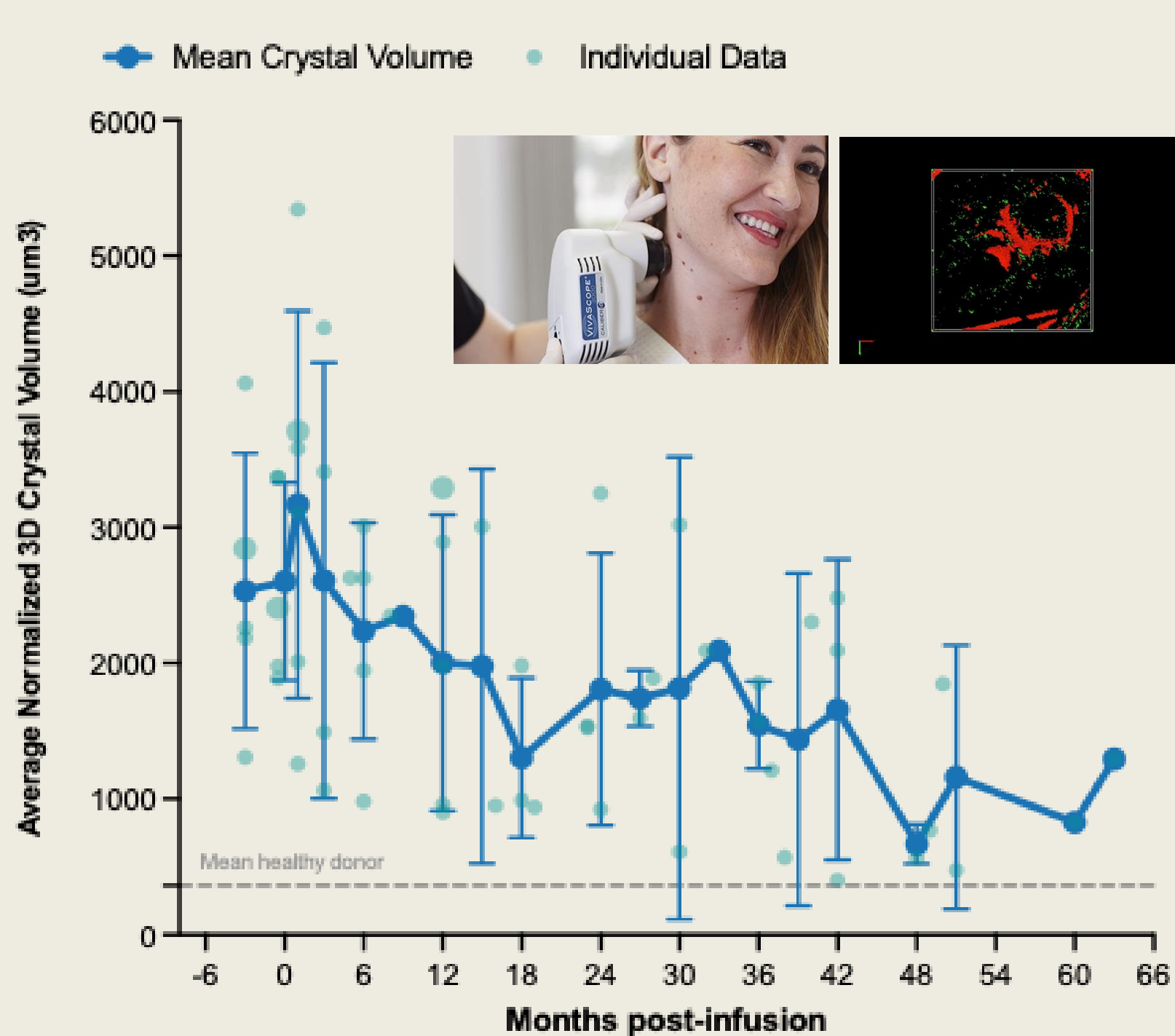
Clinical Trial
Start Date



6 adult patients with cystinosis
(5 men and 1 woman)



Barshop *et al.*, NEJM 2026

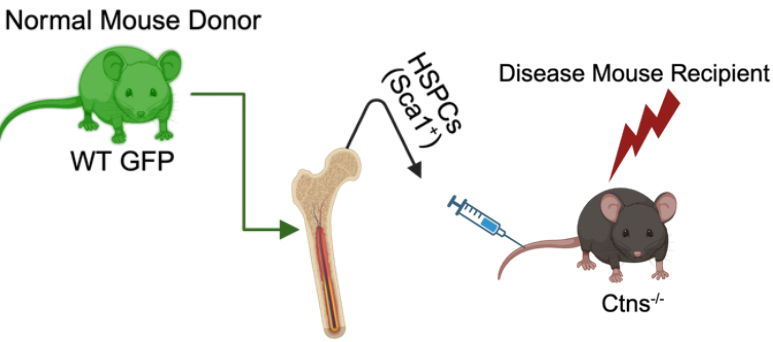


DRUG DEVELOPMENT TIMELINE

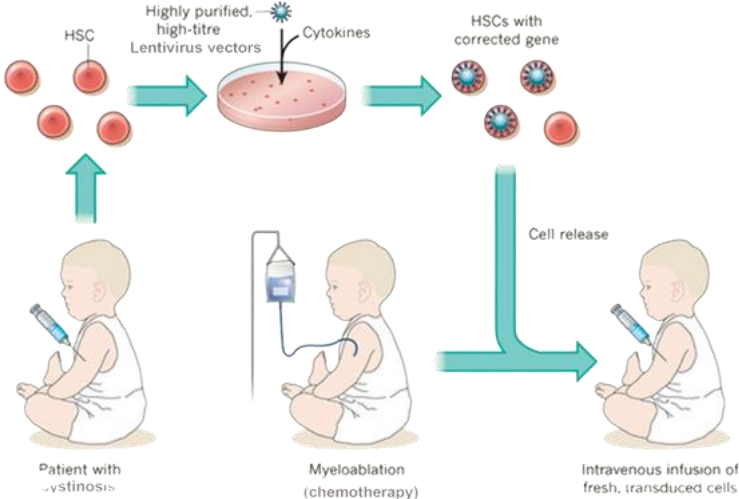
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NOVARTIS

PRE-CLINICAL STUDIES



TRANSLATIONAL DEVELOPMENT



ADULT CLINICAL TRIAL



PEDS CLINICAL TRIAL



Proof of Concept

FDA

Interact Meeting

FDA

Pre-IND Meeting

UC San Diego

Safety Studies
Manufacturing Development

FDA

Phase ½ -IND Allowance

The NEW ENGLAND
JOURNAL of MEDICINE

- **2019:** 1st Patient Dosed
- **2022:** 6 Patients Treated
- **2022 - Present:** Long-term follow-up of adult patients

- **2025 - Present:** Phase ½ - Pediatric Trial Open
- **2026:** 1st Peds Patient Dosed

2007 2012 2013 2014 - 2017 2018 2019 - 2026

PRE-CLINICAL STAGE

CLINICAL STAGE

Early-Stage Grant
Funding

2016:
CLIN-1 Funding

2017:
Sub-license

2019:
CLIN-2 Funding

2023:
Acquisition

cystinosis
RESEARCH FOUNDATION

NIH
National Institutes
of Health

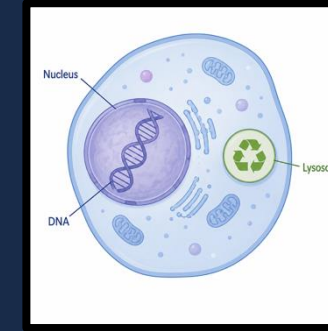
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NOVARTIS

GAME-CHANGING DISCOVERY



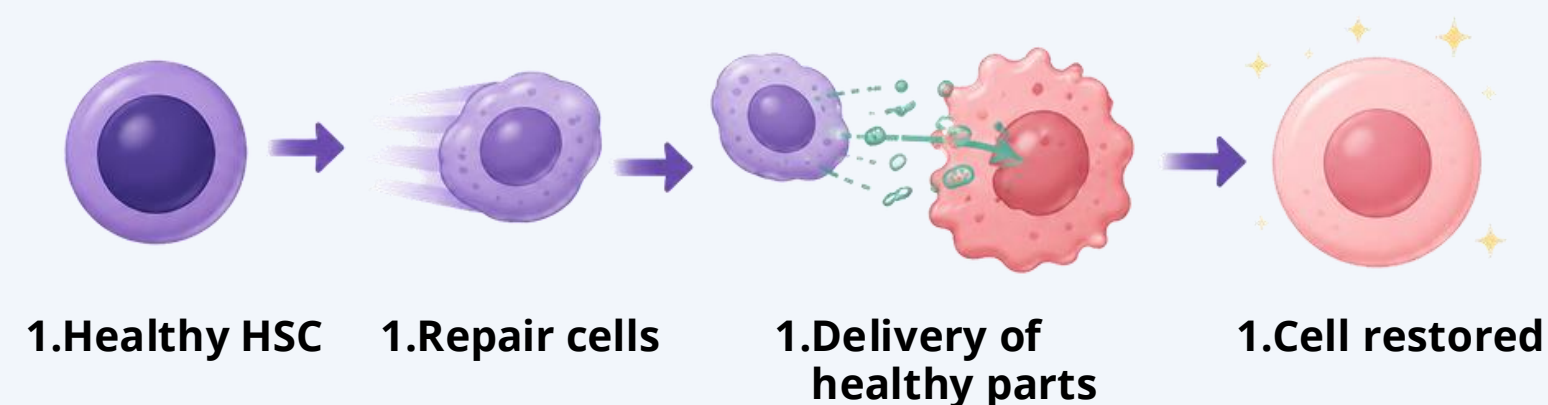
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WE IDENTIFIED THE DELIVERY VEHICLE THAT RESCUES CELLS

Macrophages derived from Hematopoietic Stem Cells (HSCs)

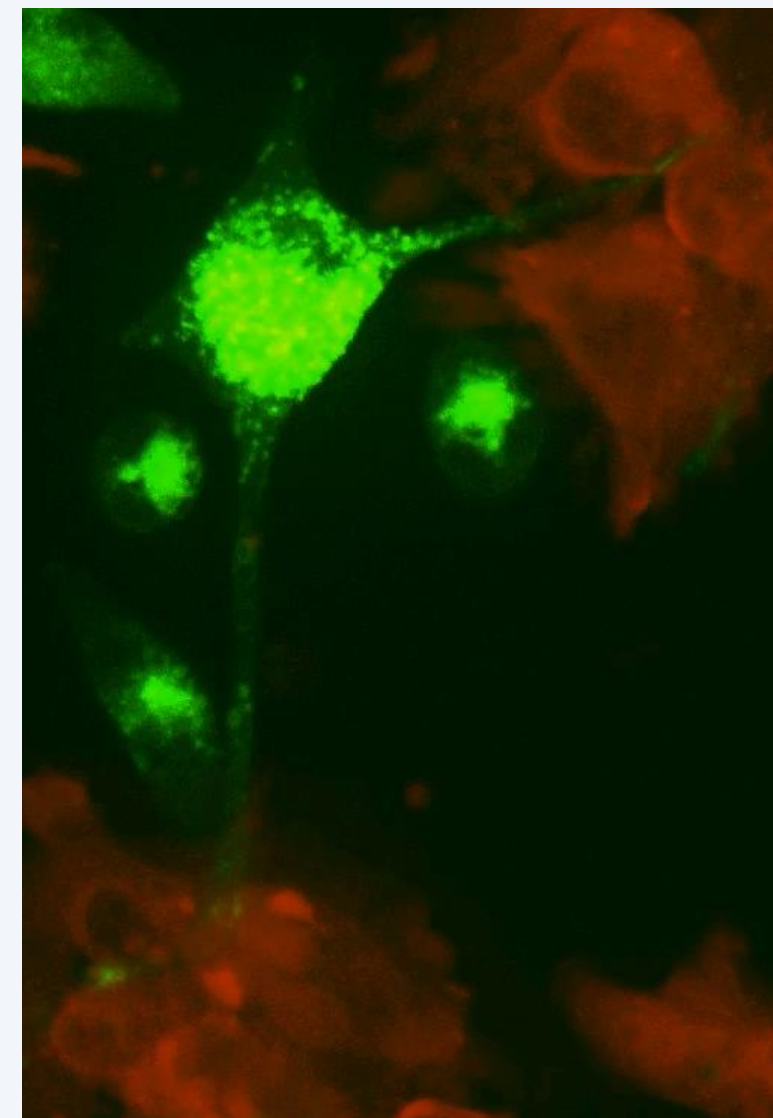
Cells produced by healthy **Hematopoietic Stem Cells (HSC)** can find damaged cells in the body and deliver healthy parts directly to them.



CTNS-eGFP = A fluorescently tagged version of the cystinosis protein



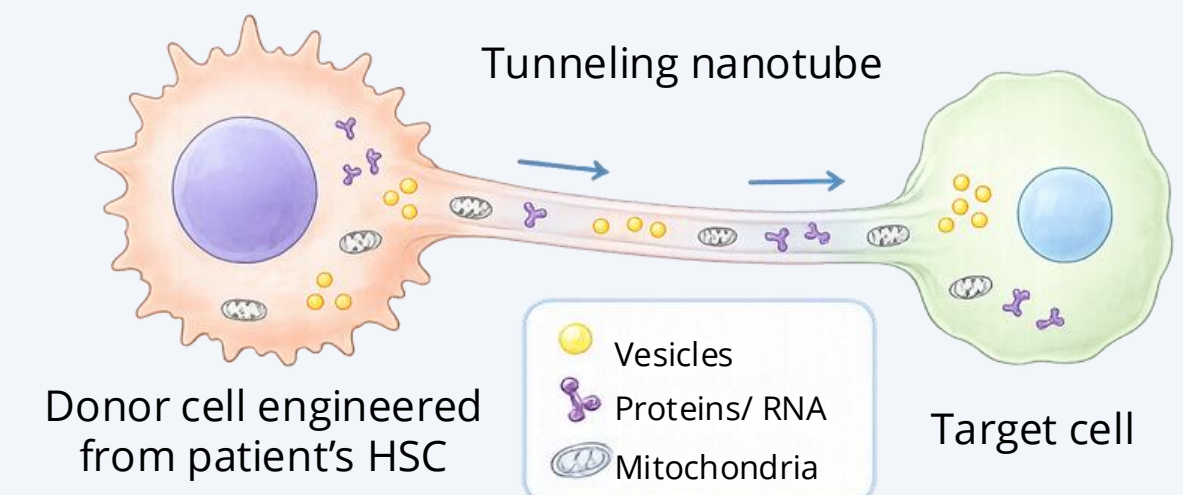
MECHANISM OF ACTION



Macrophage Tunneling Nanotubes (TNTs)

Macrophages made from modified hematopoietic stem cells (HSCs) travel through the body and repair damaged cells by sending healthy parts through tiny cellular "highways."

HSC rescuing a diseased cell



Treating Other

LYSOSOMAL DISORDERS

DYSFUNCTIONAL LYSOSOMAL TRANSMEMBRANE PROTEINS



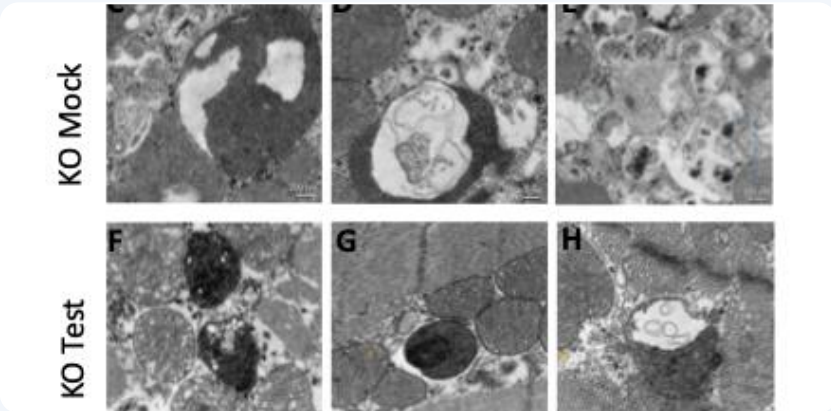
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No FDA approved treatments



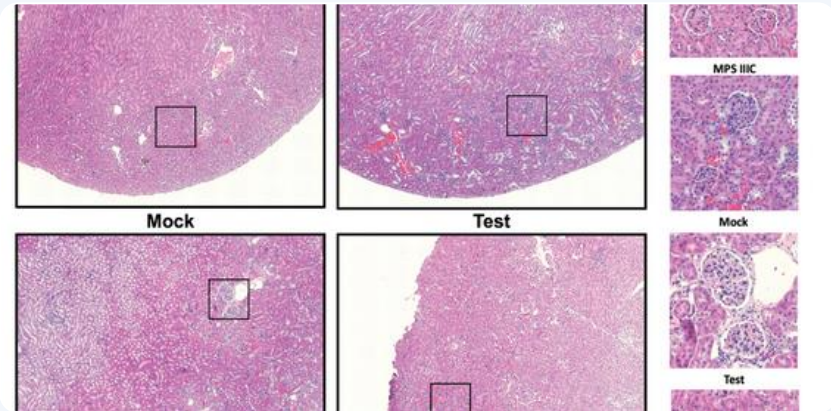
Eric Adler, MD
Cardiologist, UC San Diego

DANON DISEASE - LAMP2B PROTEIN



Causes severe cardiomyopathy, muscle weakness, and developmental delays, often leading to early heart failure.

SANFILIPPO SYNDROME TYPE C - HGSNAT PROTEIN



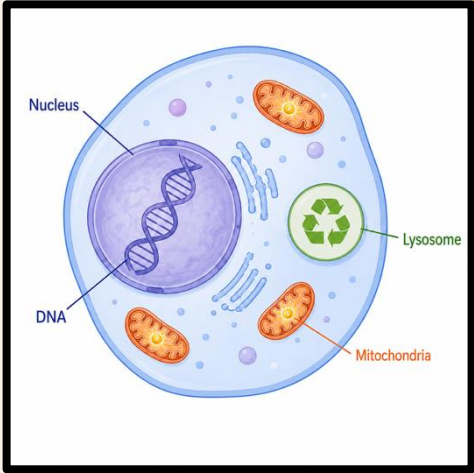
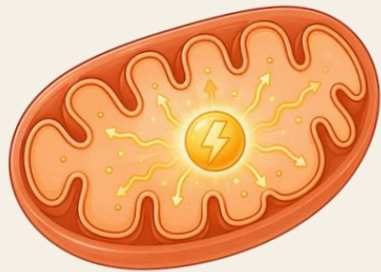
Causes progressive neurodegeneration due to impaired cellular waste breakdown, leading to severe cognitive and motor decline in childhood.



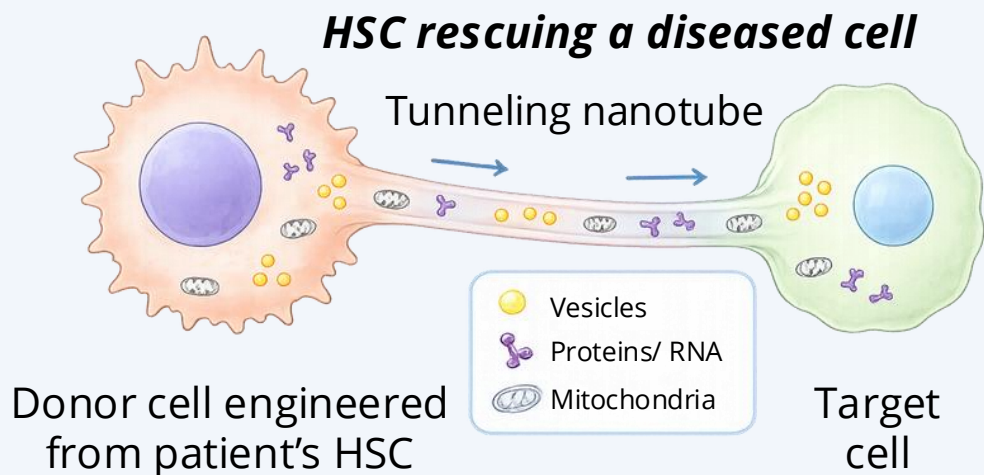
Current Status: Entering the planning phase for transition into clinical trials.

About

MITOCHONDRIAL DISEASES



 **MACROPHAGES CAN DELIVER HEALTHY MITOCHONDRIA TO DAMAGED CELLS**



Friedreich's Ataxia is an inherited **mitochondrial disease** caused by a defective **Frataxin** protein.

The Frataxin protein helps mitochondria produce energy.

No effective treatments to date

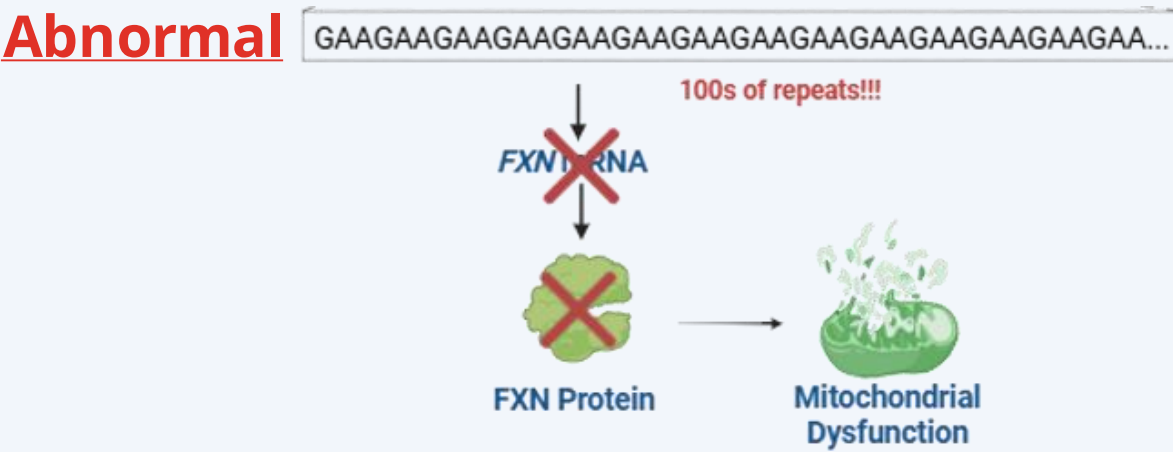
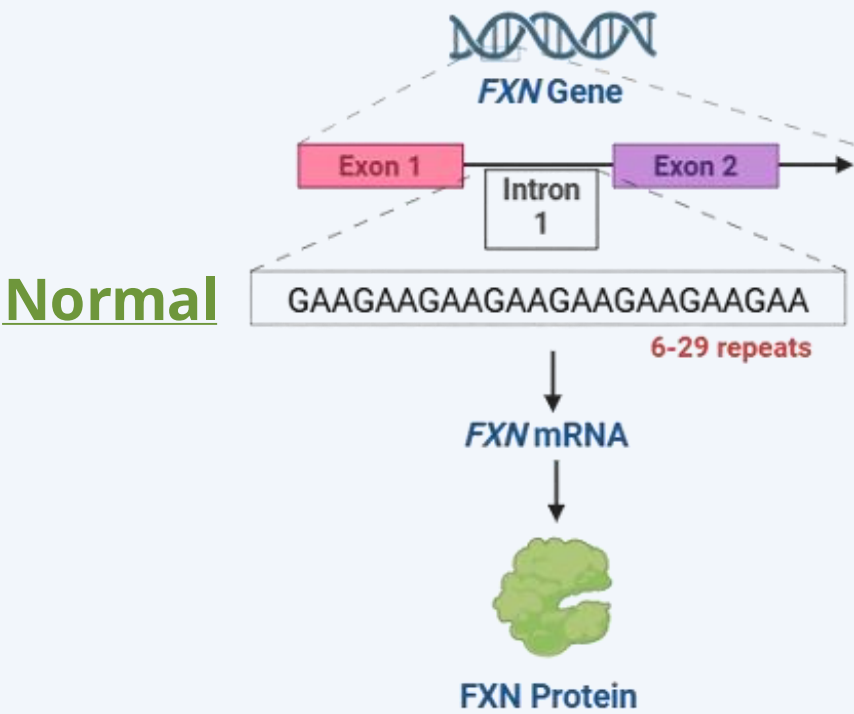
FRIEDREICH'S ATAXIA (FA)



A progressive neuromuscular degenerative disease characterized by the gradual loss of motor function. Patients typically become wheelchair-bound and often succumb to complications related to heart defects

NO EFFECTIVE TREATMENT

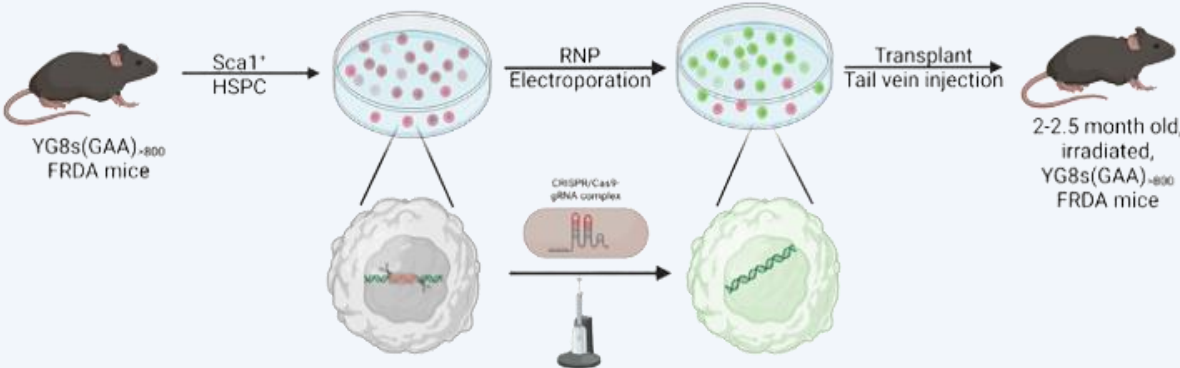
Diseased cells have too many **GAA repeats** in the **FRATAXIN** gene.



CRISPR/CAS9 GENE EDITING

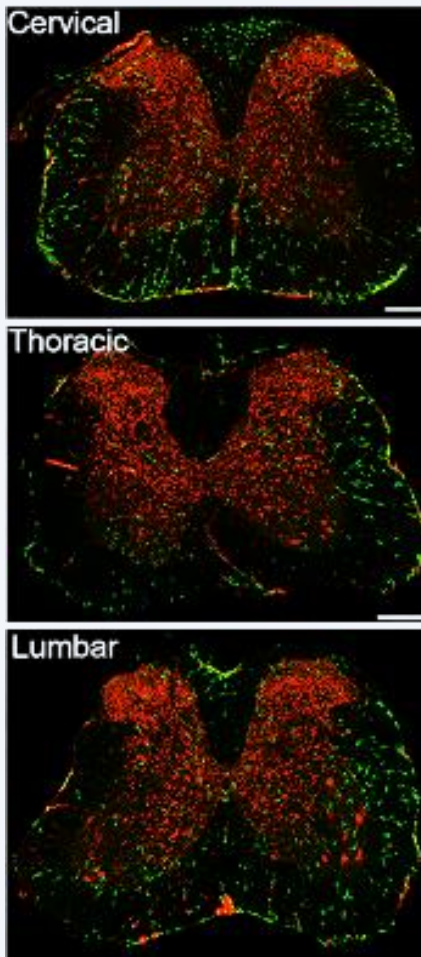
for Friedreich's Ataxia

PRE-CLINICAL STUDIES



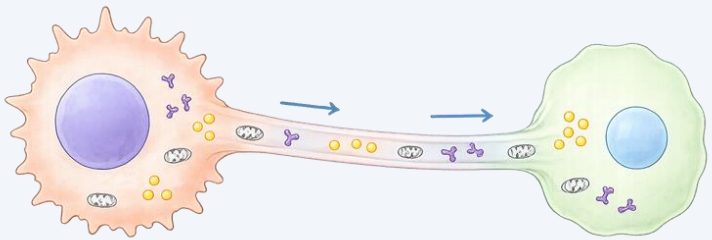
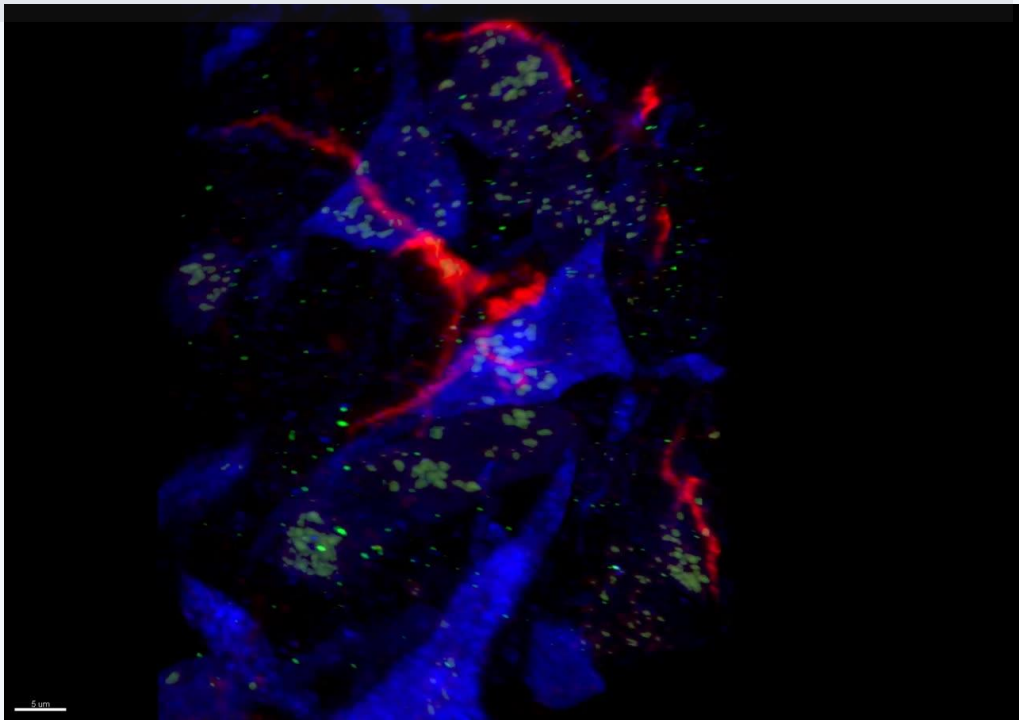
PREVENT NEURON DEATH

SPINAL CORD

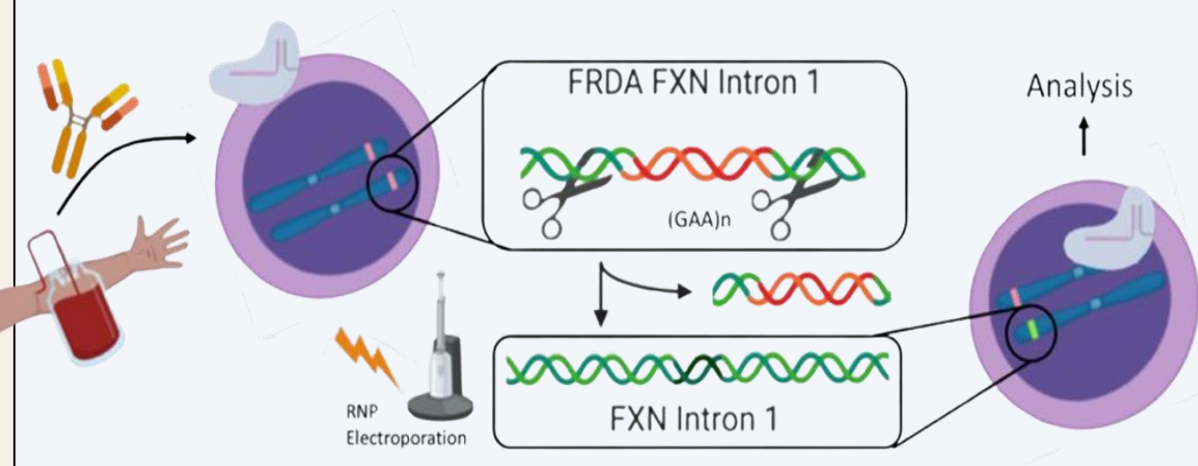


BRAIN

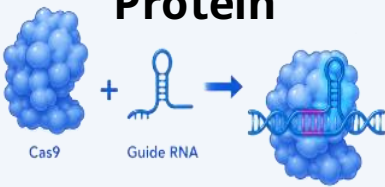
Healthy microglia help survival of neurons



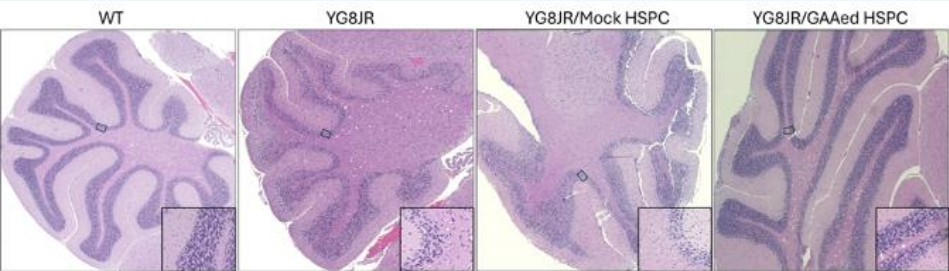
CD34⁺ HSPC from FA patients



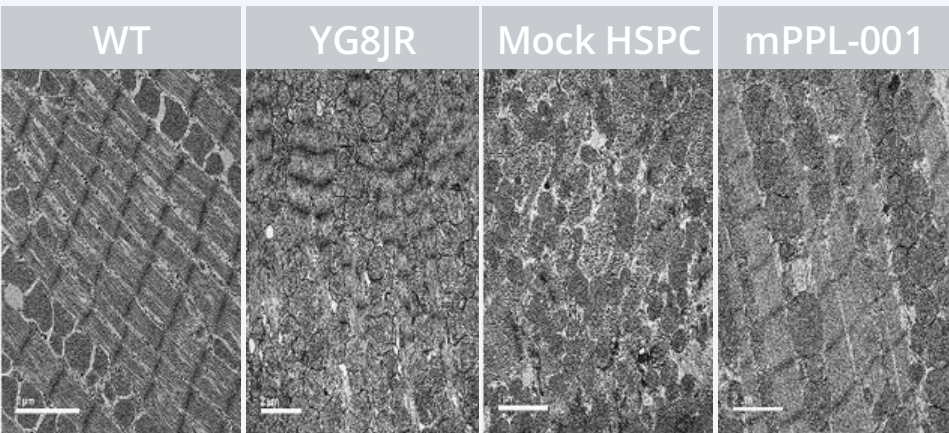
CRISPR/CAS9 Protein



PREVENT NEURONAL DEATH

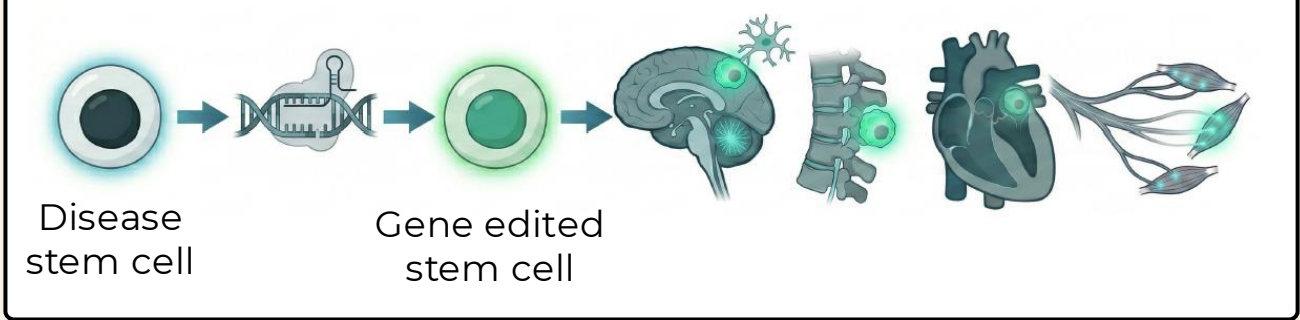


RESCUE THE HEART DEFECTS

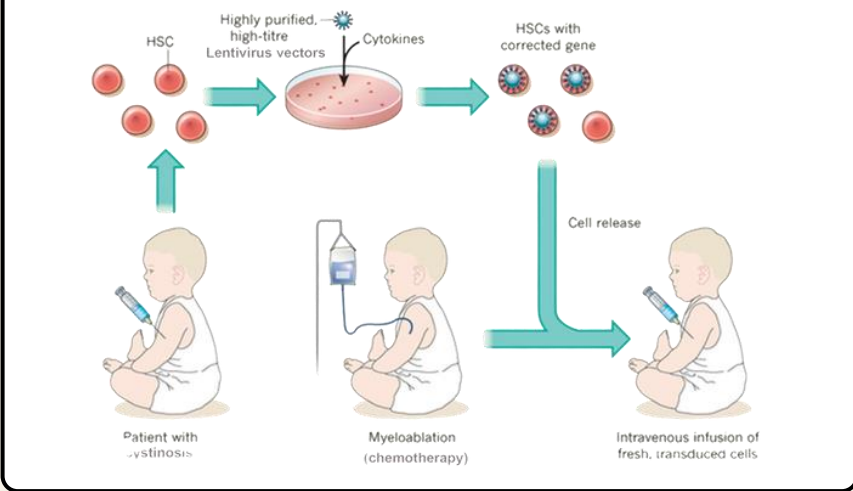


DRUG DEVELOPMENT TIMELINE

PRE-CLINICAL STUDIES



TRANSLATIONAL DEVELOPMENT



GFP HSC → FRDA mouse model

Proof of Concept

FDA

Interact Meeting

FDA

Pre-IND Meeting

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- Pharmacology
- Toxicology Studies
- Scale-up Manufacturing

FDA

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- Submit IND Application
- Review/Approvals
- Start of Clinical Trial (Phase 1)

2017

2023

2024

2026

FUTURE PLANS

PRE-CLINICAL STAGE

CLINICAL STAGE

Early-Stage Grant Funding

2023:
TRAN-1 Funding

2026:
PDEV Funding

GAME-CHANGING DISCOVERY

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MICROGLIA DRIVE NEURON DESTRUCTION IN FA

Microglia are the brain's immune cells which protect and clean the brain.

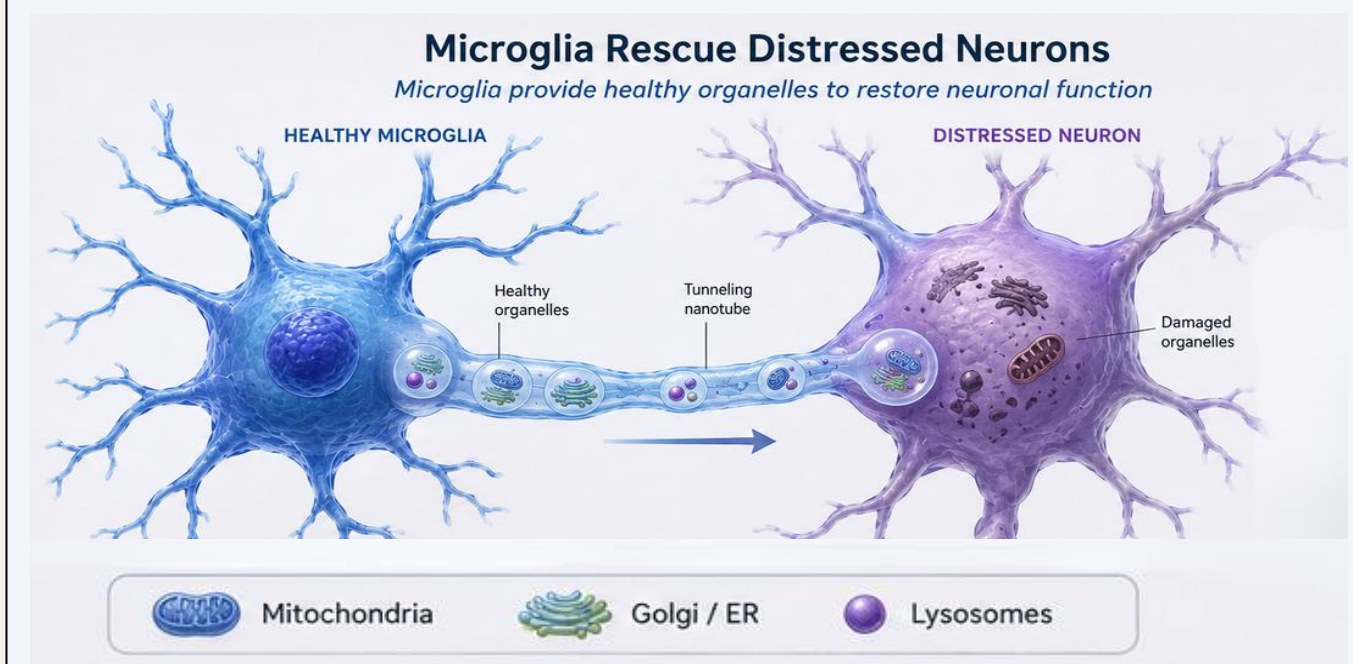
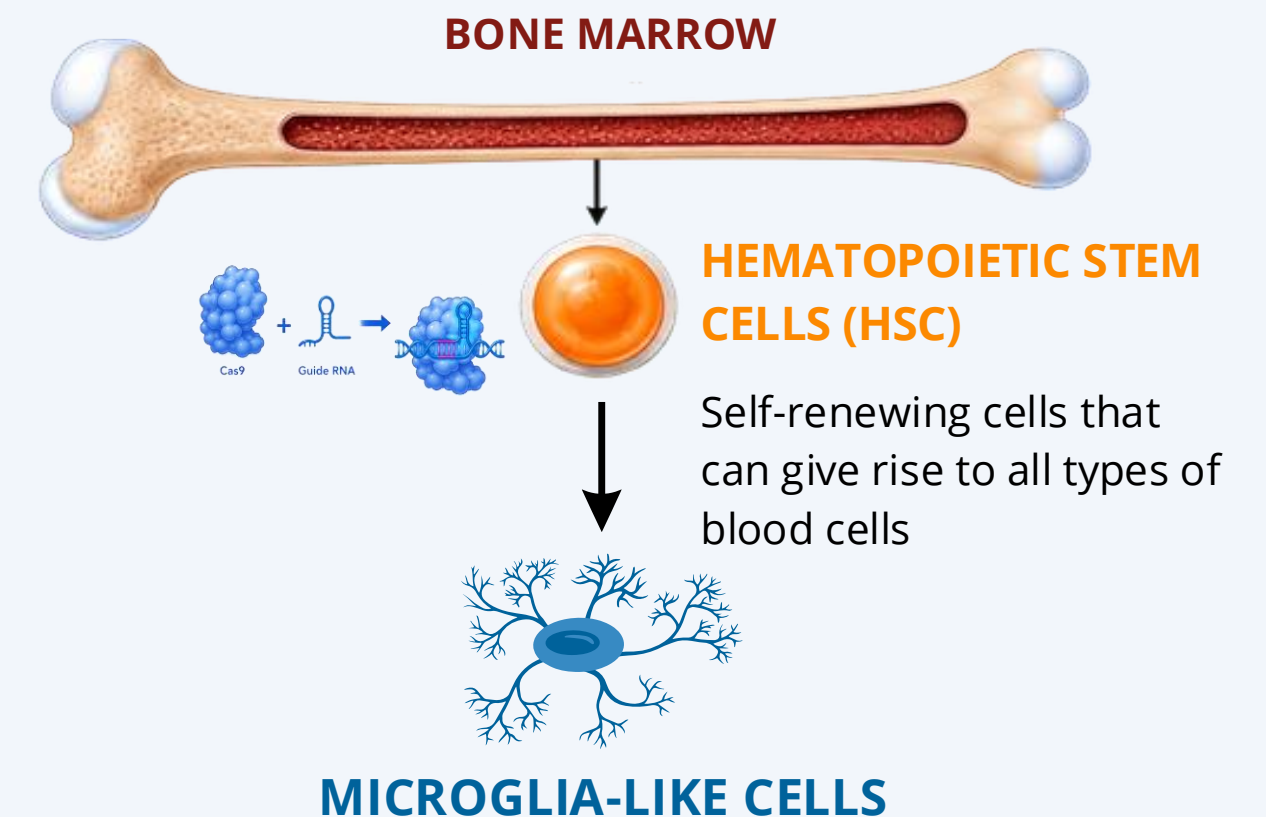
In FA the microglia are inflamed, instead of just reacting to damage.

INFLAMED MICROGLIA



ACTIVATED IN DISTRESS

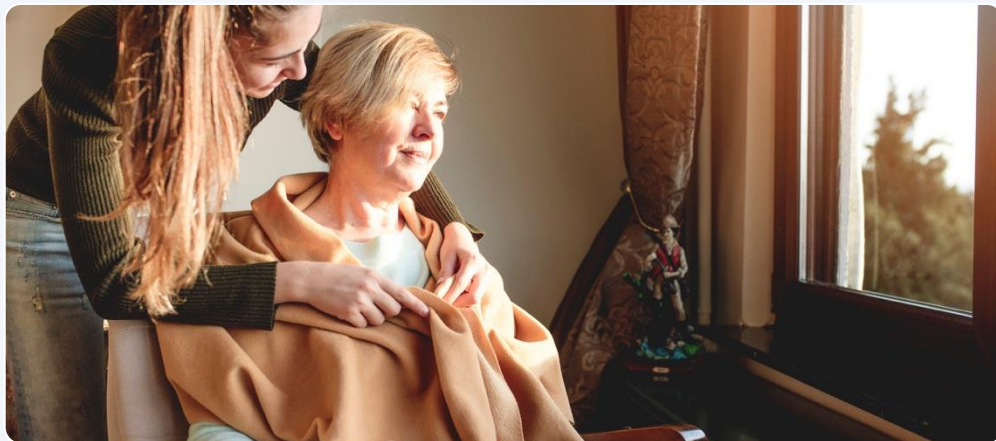
Inflamed microglia actively drive the destruction of healthy neurons and become a primary cause of the disease.



Application to ALZHEIMER'S DISEASE



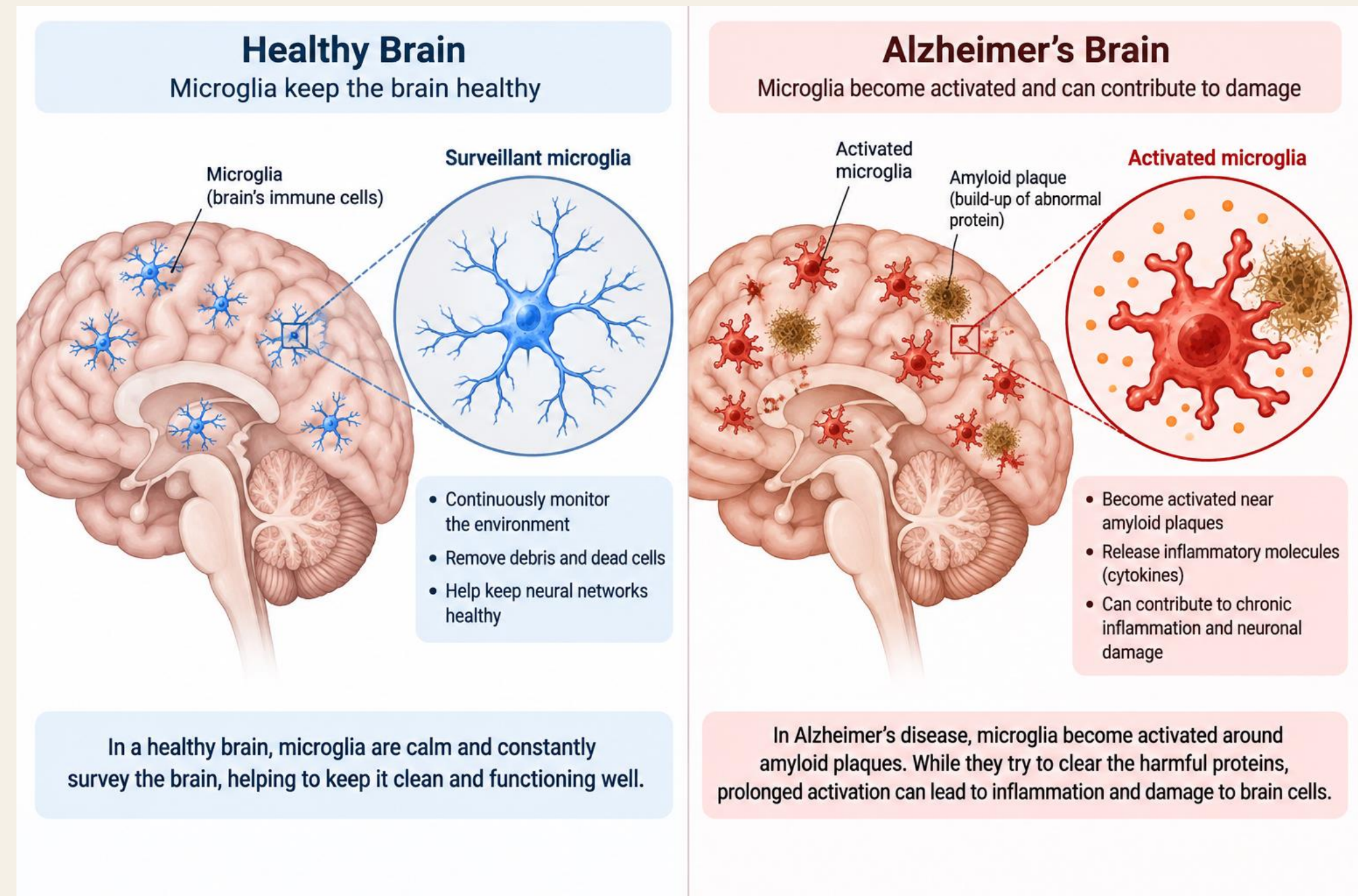
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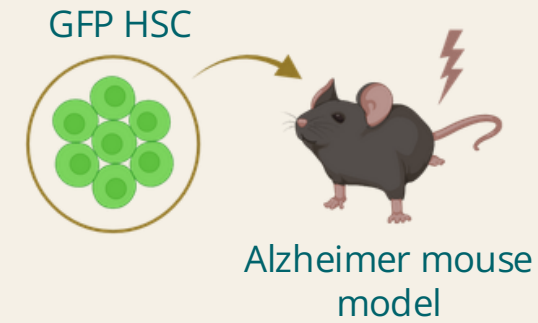
Abnormal proteins build up in the brain, damaging neurons and causing memory loss, cognitive decline, and changes in behavior.

Research has focused targeting the abnormal protein build up.

However, recent findings show that **microglia may also drive the disease.**

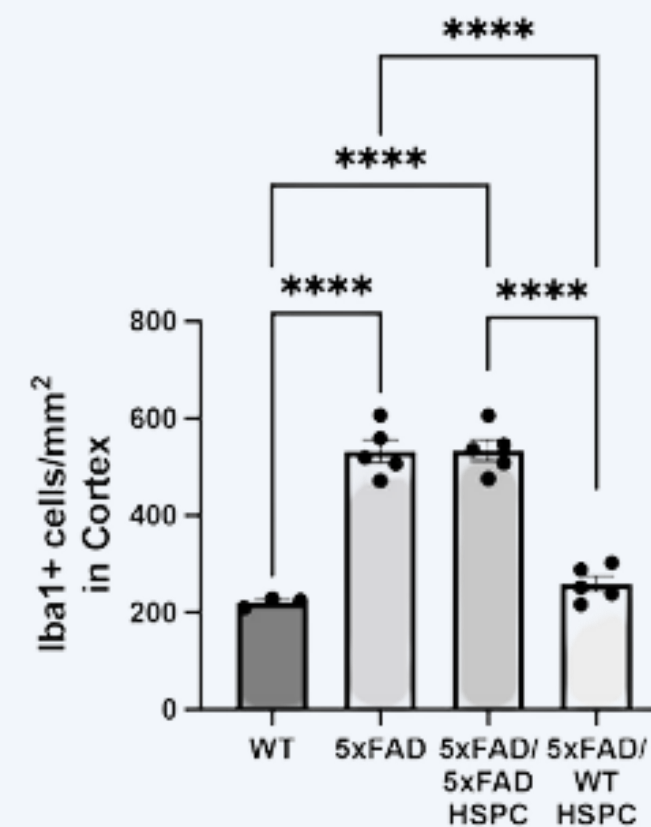
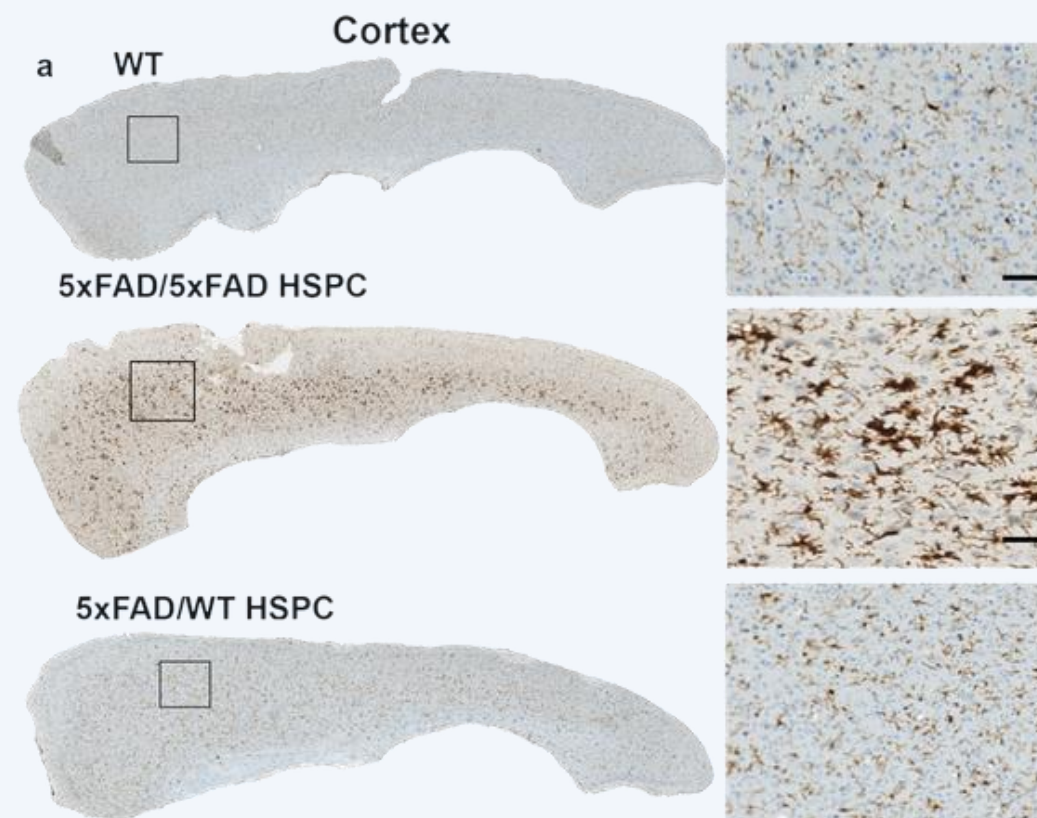


About ALZHEIMER'S DISEASE



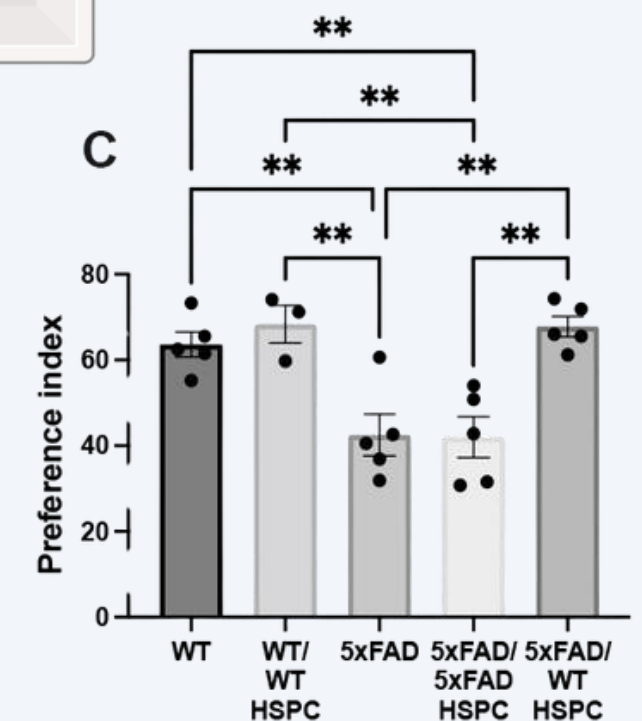
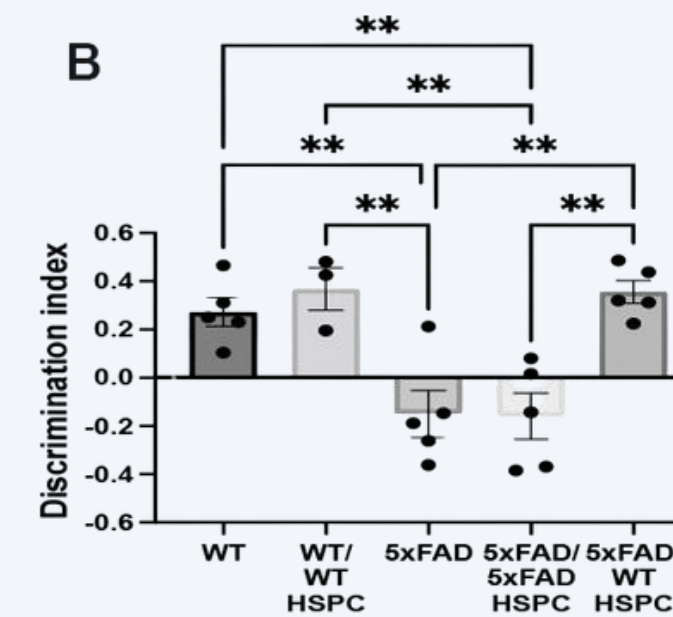
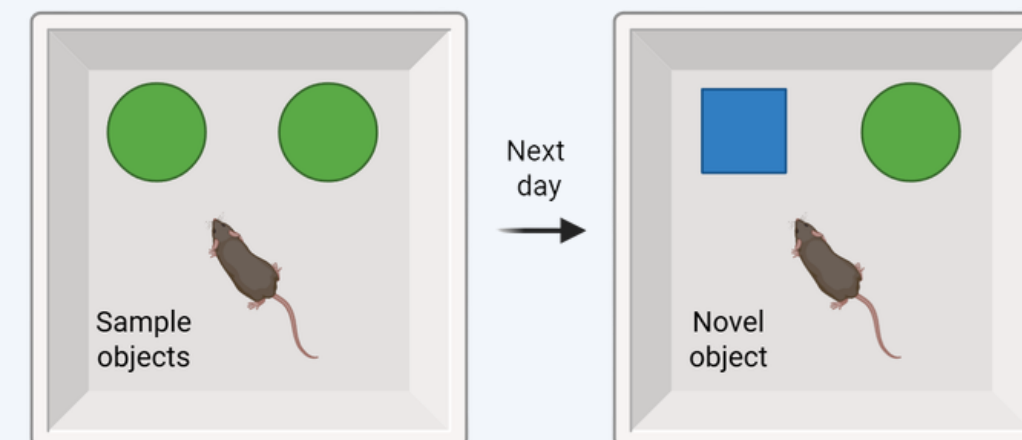
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BRAIN SECTIONS SHOWING INFLAMMATION IN MOCK-TREATED ALZHEIMER MICE AND RESCUE IN THE MICE RECEIVING WILDTYPE HSC



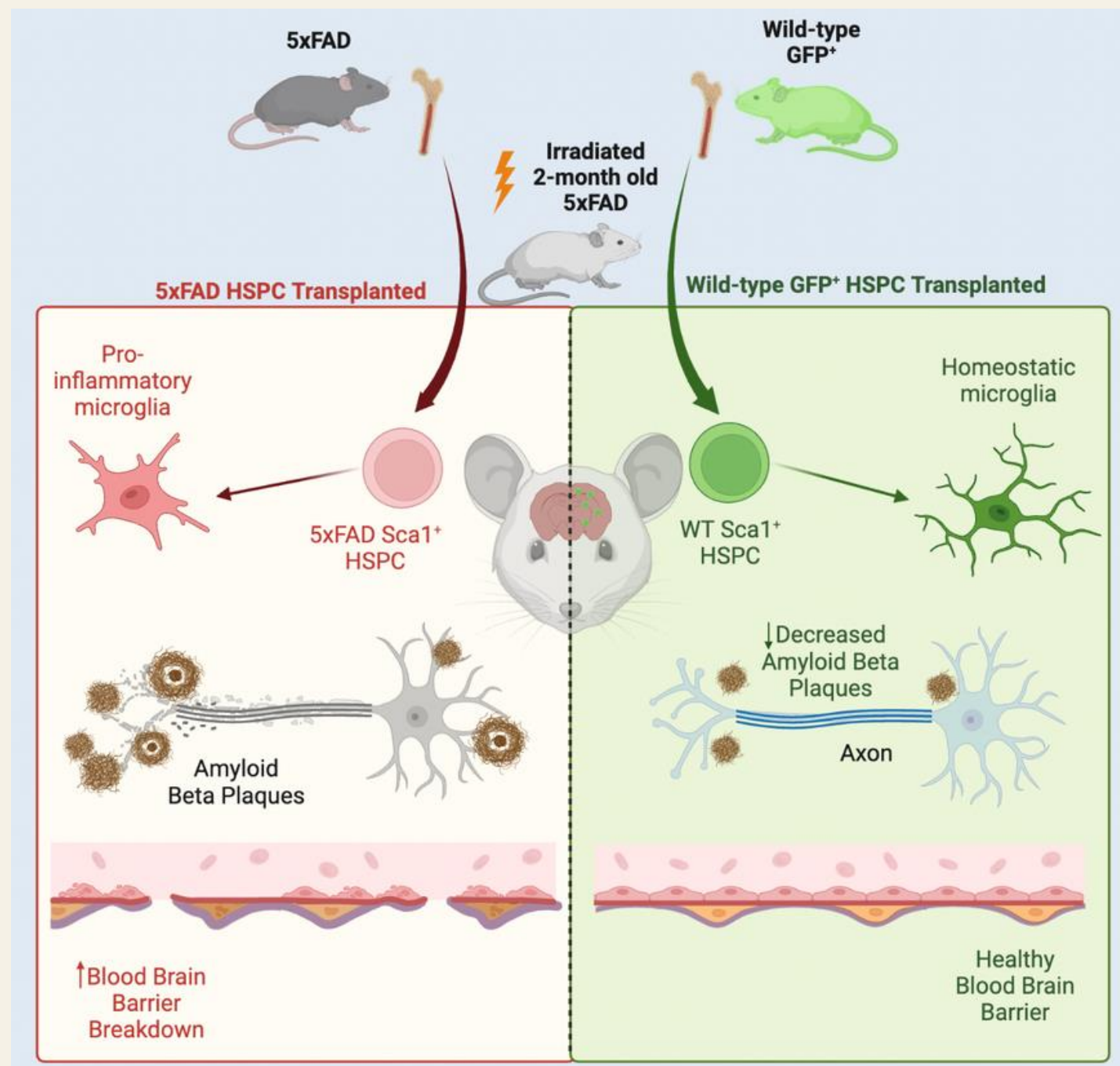
NOVEL OBJECT RECOGNITION TEST: TEST FOR COGNITIVE FUNCTION AND MEMORY

More time exploring the novel object = mouse remembers the familiar object and can discriminate between the two

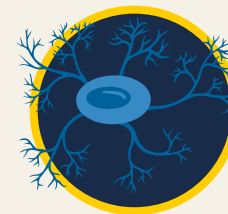


GAME-CHANGING DISCOVERY

& NEXT Steps



Hematopoietic Stem Cells & Gene Therapy provide:



Healthy Microglia like cells that stop the inflammation in the brain and prevent the destruction of neurons

→ **NEXT STEPS**

UNDERSTAND THE MECHANISM

of Alzheimer's Disease rescue by WT hematopoietic stem cells

DEVELOP EX VIVO HEMATOPOIETIC STEM CELL GENE THERAPY

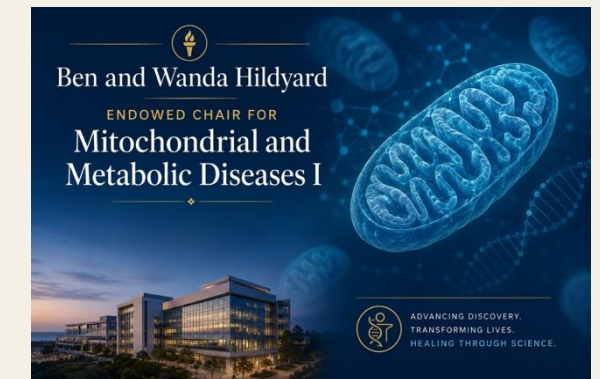
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Maxwell Okros

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Belle Pan

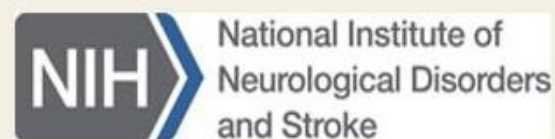


SPECIAL THANKS

to the Patients
& their families



**The Cystinosis Stem
Cell Gene Therapy
Consortium**



Medical Staff

Collaborators

