Gene Therapy – Access to Innovative Therapies for Rare and Ultrarare Disorders

Women in Government Leadership & Innovation Summit

November 15, 2024

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Introductions

Rep. Donna White
State of North Carolina
NC Life Sciences Caucus
Co-Chair

Moderator

Steven Gray, PhD
University of Texas Southwestern Medical Center
Director, Gene Therapy Program
Professor, Dept. of Pediatrics

Gene Therapy 101

Josh Argall
Devin's Father
WI Rare Board Member
Patient Advocacy Strategies
VP, Engagement & Operations

Patient and Family Perspectives

Erin Frey
Ultragenyx
Senior Director
State Government Affairs

State Policy Considerations

What is Gene Therapy? Gene Therapy 101

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UT Southwestern Medical Center

Gene Therapy: Emerging Transformative Paradigms for Treatment of Human Disease

Steven Gray, Ph.D.
Professor of Pediatrics, Molecular Biology, and Neurology
Eugene McDermott Center for Human Growth & Development
Director, UT Southwestern Viral Vector Facility
Director, UT Southwestern Gene Therapy Program

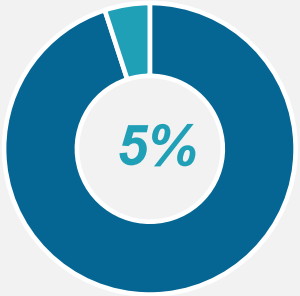
Any stated opinions are Dr. Gray's own, and not necessarily representing UTSW.

The **HUMAN GENOME** has approximately **20,000** genes

More than **6,000** diseases are caused by genetic mutations

Many are **RARE** diseases affecting 30 million Americans *(1 of 10)*

ONLY **5 percent** of these diseases have **APPROVED** therapies



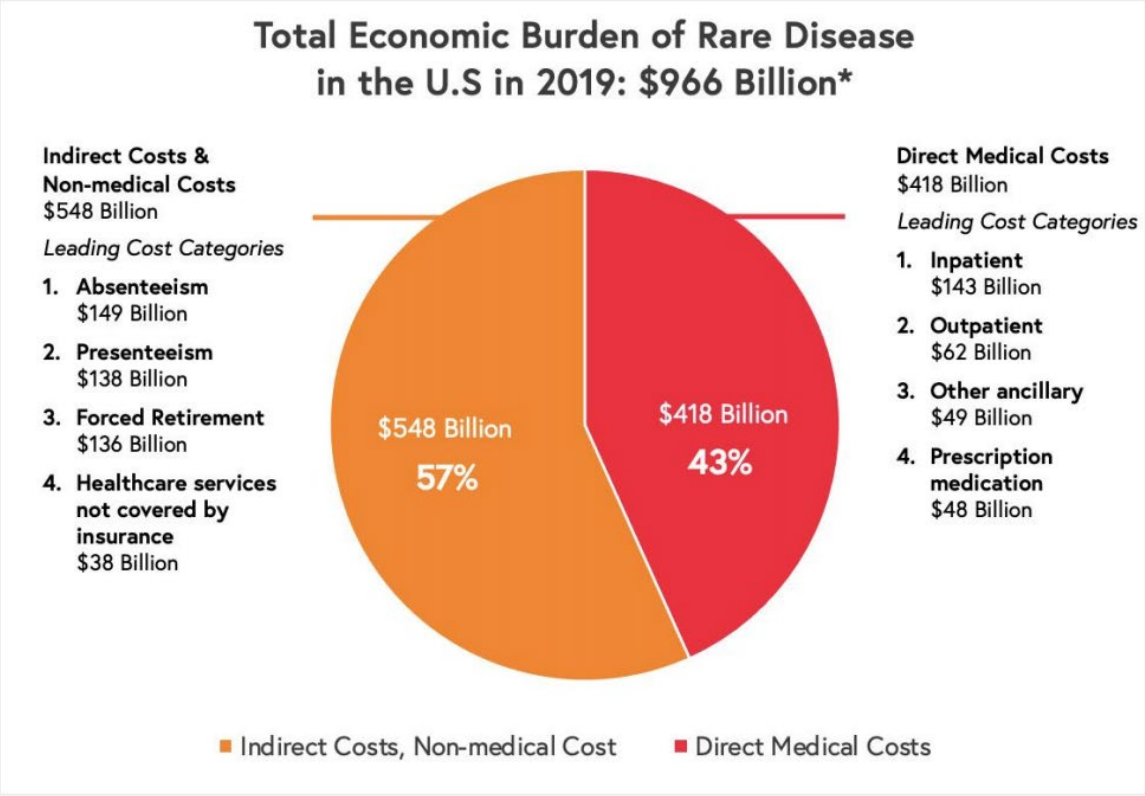
CBS NEWS NEWS SHOWS VIDEO CBSN MORE

FDA approves gene therapy for rare form of blindness

FORTUNE

The Way We Treat Cancer Will Be Revolutionized as Gene Therapy Comes to the U.S.

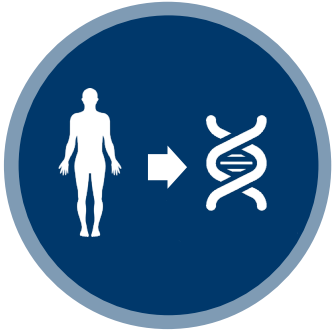
“Rare” Genetic Disease – a large but hidden problem



Source: EveryLife Foundation, published Feb 25, 2021

Broken Genes Lead to Broken Proteins

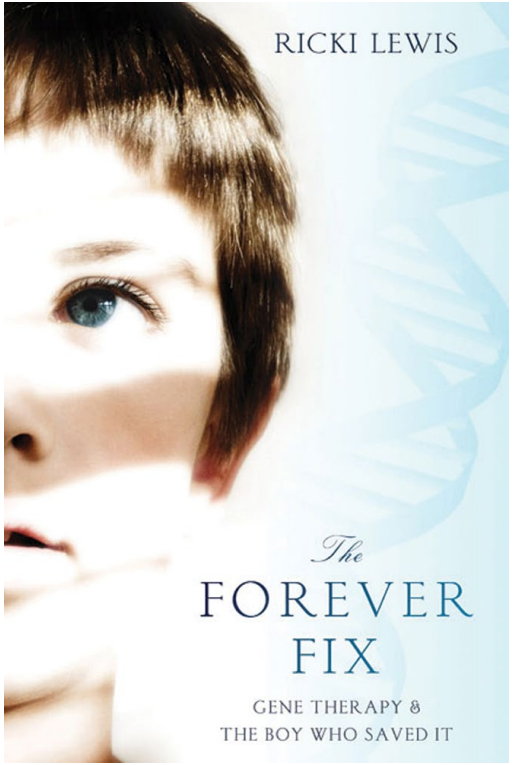
Humans are made of cells that contain our **genes**



Genes are instructions for **proteins**

Proteins help **cells** function in a healthy manner

Abnormalities in genes can result in proteins that do not function properly

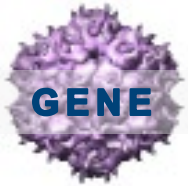


The promise of **gene therapy** is to fix a genetic disease at the source.

If you fix the DNA, you've solved the problem permanently.

How Does Gene Therapy Work?

Identify the causal defective gene



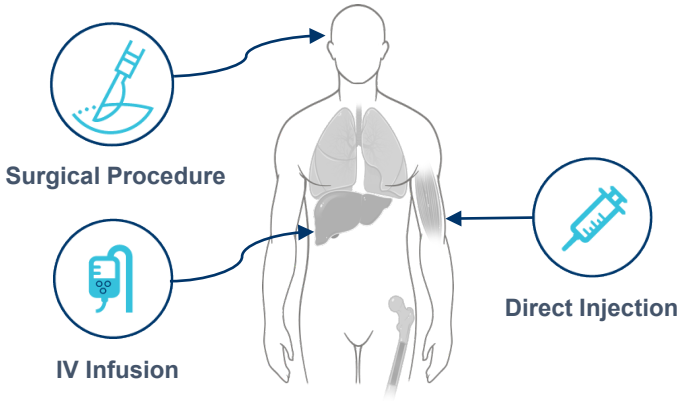
Package a ***working*** copy of the gene into a carrier like an engineered virus

Deliver the working copy of the gene back into the patient

Gene Therapy: Treating Patients

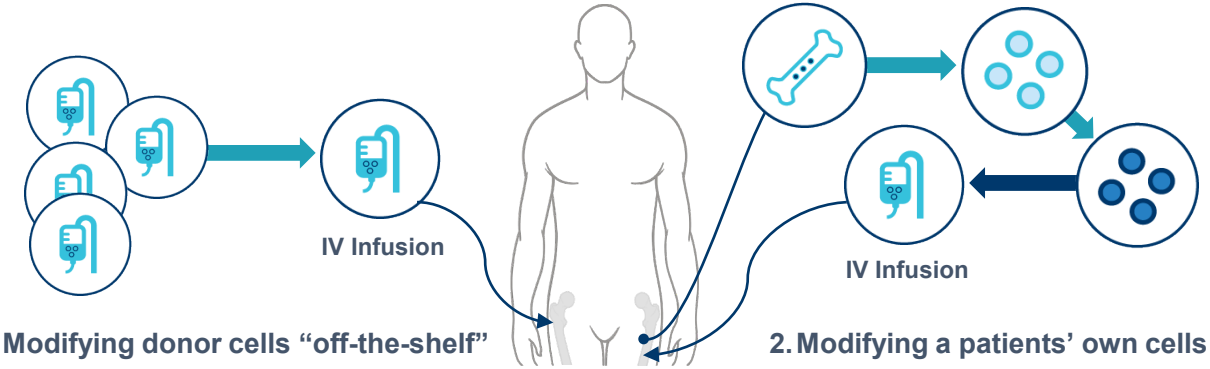
In Vivo Approaches

- Intervene inside the body
- Genome modifications within target cells after individuals receive a genomic medicine
- e.g., surgery, injection

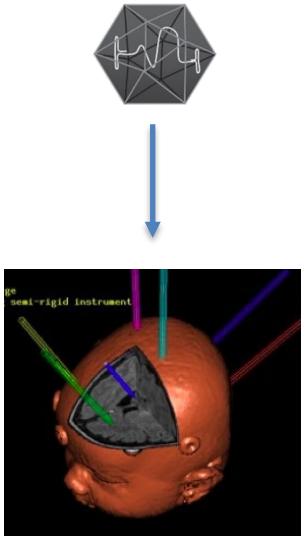


Ex Vivo Approaches

Outside the body,
create cell medicines by:



AAV Gene Therapy for AADC Deficiency



Sci Transl Med. 2012 May 16;4(134):134ra61.

Gene therapy for aromatic L-amino acid decarboxylase deficiency.

Hwu WL, Muramatsu S, Tseng SH, Tzen KY, Lee NC, Chien YH, Snyder RO, Byrne BJ, Tai CH, Wu RM.

Krabbe Disease

Affects ~1:100,000 children

Symptoms start at ~6 months

Typically fatal by 1-3 years old.

Jim and Jill Kelly with their son Hunter in 2004. Hunter, who had Krabbe disease, died in 2005 at age 8.

Don Heupel/AP

https://www.npr.org/sections/health-shots/2013/12/18/255226663/screening-newborns-for-disease-can-leave-families-in-limbo

Treatment of Dogs With Krabbe Disease

“Placebo” – 10 weeks old

Treated – 70 weeks old

Bradbury et al, Journal of Clin Inv, 2020

Patients that deserve a better future

Exciting gene therapy technologies

Why aren't these two things coming together more?

Not enough patients for pharma involvement

Preclinical IND-enabling

Initial Clinical Trial

Pivotal Clinical Trial

BLA

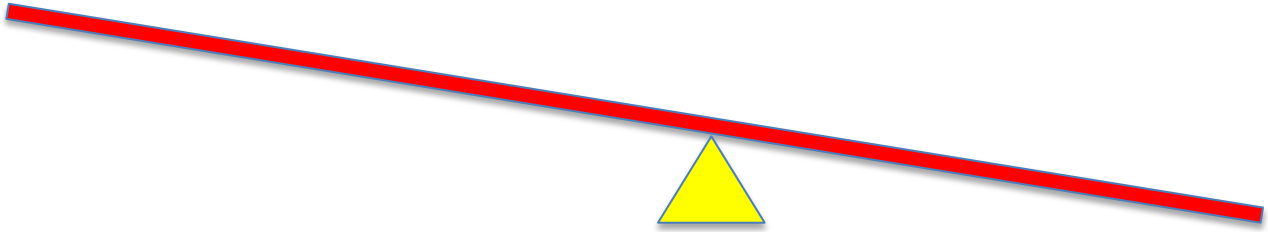
Approved Treatment

Private Foundations / Government / Philanthropy

Commercial Partners

COST / RISK

REIMBURSEMENT



Regulating Genomic Medicine

- Regulation of gene & cell therapies are governed by the U.S. Department of Health & Human Services HHS (FDA & NIH)
- FDA treats all genome edited cells as medical products
- Federal law prohibits the FDA from reviewing INDs using human germline cells and prohibits the NIH from funding research in germline cells
- FDA prohibits the conduct of clinical trials using germline editing

Regulating Gene & Cell Therapy Products

- FDA has an established regulatory framework to regulate cell and gene therapy products
- FDA has recently developed new regulatory programs to help expedite review of cell and gene therapy products:
  - INTERACT
  - RMAT
- Cell and gene therapy products must fulfill the same evidentiary standards to prove safety and efficacy as any other FDA-approved drug

Sources:
FDA. *Human Gene Therapy for Rare Diseases: Draft Guidance for Industry*. July 2018.
FDA. *Testing of Retroviral Vector-Based Human Gene Therapy Products for Replication Competent Retrovirus During Product Manufacture and Patient Follow-up; Draft Guidance for Industry*. July 2018
FDA. *Long Term Follow-up After Administration of Human Gene Therapy Products; Draft Guidance for Industry*. July 2018.

Thank You

Josh’s kids:
Benny
Devin
Genevieve

State Policy Considerations

A Few Words on Pricing:
Cost Conscious, Patient-Centered, Worldwide Access

Elements that impact gene therapy pricing

- Clinical
  - Clinical trial designs and endpoints
  - Small populations
  - Probability of success
- Manufacturing practices
  - In-house or outsource
  - Cost of goods
- Improved science/processes over time.
- Pricing for majority access vs. other approaches.
- Value to patients and their caregivers/families.

Ultragenyx Gene Therapy Manufacturing Facility

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State Policy that impacts the Rare Disease Community

Economic Development

- Focus on inviting life science, biotech and medical innovation companies into your state.
- Incentivize innovation with R&D tax credits

Earlier Diagnosis

- Newborn screening parity with the Recommended Uniform Screening Panel
- Rapid Whole Genome Sequencing Coverage
- Biomarker Testing Coverage

Access to Treatments

- Copay Accumulator Ban
- Prior Authorization reform
- Ensure any legislation appropriately recognizes rare disease
- Ensure Medicaid adds utilization criteria for new treatments swiftly

Hear the Rare Voice

- Rare Disease Advisory Council
- Form a Rare Disease Caucus
- Ensure Medicaid includes rare experts and patient advocates in the Drug Utilization Review and Prescriptions & Therapeutics boards

Questions?

Panelists' Contact Information:

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