Rare Disease Day Program

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“Rare” Diseases

Rare until it happens to you, someone you know, or your child

Rare unless you are at the University of Minnesota

We may be Rare but we've got ROAR!

- JULIE FLYGARE, NARCOLEPSY SPOKESPERSON

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Abeona Therapeutics

University of Minnesota Masonic Children's Hospital

Children's Cancer Research Fund

Center for Genome Engineering

Agathos Biologics

Jimbo & Candi Fisher Kidz 1st Fund

Join in the Fight Against Fanconi Anemia

University of Minnesota
Pediatric Blood and Marrow Transplantation

Caldevron
The basis for breakthroughs

Puck
Cures for Kids
Fanconi Anemia: a prototypical rare disease

Fanconi Anemia Comprehensive Care Program
LEADING THE NATION IN RESEARCH AND CLINICAL CARE
Multiple partners and pathways maintain the pristine architecture of the genome.
DNA Repair
Getting on Target
The Book of Life: Maintenance and Modification

Radiation kills cancer by damaging DNA

Normal          Substitution          Deletion          Inversion
BEAST  FEAST  BEST  BEATS
Gene Therapy vs Gene Editing

1. The cells are removed from the patient
2. The therapeutic gene is introduced into the cells using a delivery vehicle
3. The cells start producing the desired protein
4. The genetically modified cells are injected back into the patient
Viral Vector Adverse Events

Viral Gene Expression

Cellular Gene Expression
Base Editing vs Gene Editing

- Single
- Multi
Programmable Nuclease

Can we break and repair DNA in a cell that does not repair DNA at full capacity?
Homology Directed Repair

HDR repair

Left homology arm
Specific change
Right homology arm

Cas9-induced DSB
mRNA
Specific change introduced to the genomic DNA

Adeno Associated Virus: AAV
FA Hematopoietic Stem Cell Gene Editing

'Can't sit and wait': Gene therapy trial aims to cure rare Fanconi anemia

> 50% of the screened clones had gene correction!
Gene Editing Safety

- Each platform is based on recognizing a target sequence
- Low sequence complexity can result in ‘off target’ nuclease activity

Genome level screens for RDEB and FA candidates show highly specific reagents
Summary

• **Gene Therapy**—can achieve long term, high levels of gene expression
• Limitations are related to integration vs. non-integration
• Not subject to regulation

• **Gene Editing**—can achieve permanent & specific correction of disease causing changes to the genome
• Limitations are related to repetitive sequences
• Subject to regulation
• Excellent tool for drug/disease discovery/modeling
‘Rare’ Diseases are Pathfinders

- First gene therapy performed for a rare disease
- Invaluable for conceiving, testing, and employing next generation therapies

“When rare diseases are funded, everyone benefits!”
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Giving Hope to Families for Over 40 Years

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Using stem cell biology to change the practice of medicine.

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