



A Muscle Targeted Gene Therapy for Kennedy's Disease

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A Muscle Targeted Gene Therapy for Kennedy's Disease

Problem

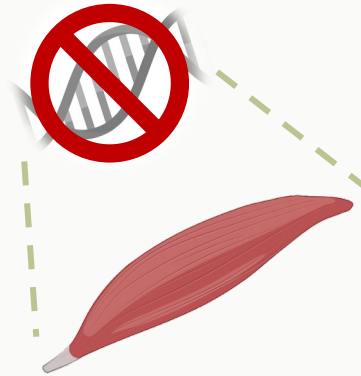
Faulty **Androgen Receptor**
gene on **X** chromosome



There are currently
NO TREATMENTS
available that address this

Solution

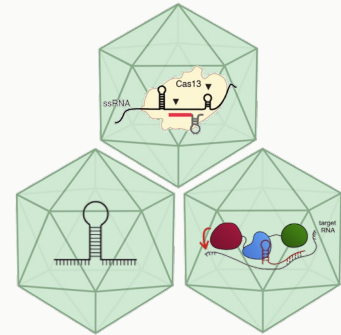
Silencing
faulty gene expression
Using
Muscle Specific
Gene Therapy



Strategy

Utilise

AAV Viral Vectors



delivering technology able to

Reduce
Androgen Receptor
Expression
in **Skeletal Muscle**



**Targeting Skeletal Muscle
(And Avoiding Other Tissues)**

A large, thick red arrow pointing downwards, with a red, textured circular outline around its shaft. The arrow is positioned to the right of the text "Reducing Expression of Androgen Receptor".

**Reducing Expression of
Androgen Receptor**



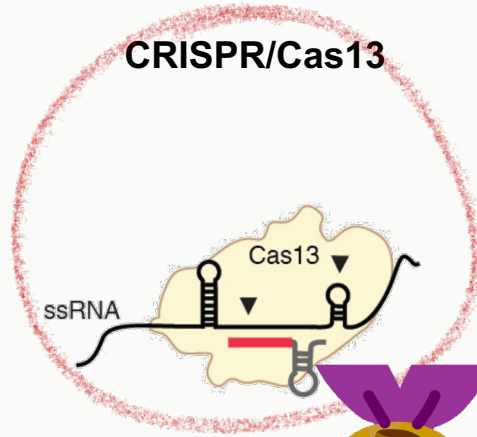
**Reducing Expression of
Androgen Receptor**

Three Gene Silencing Approaches to reduce expression of Androgen Receptor

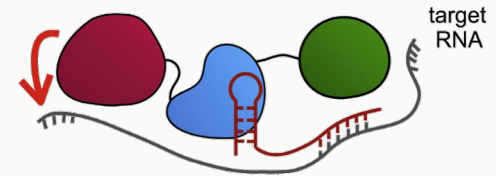
shRNAmir



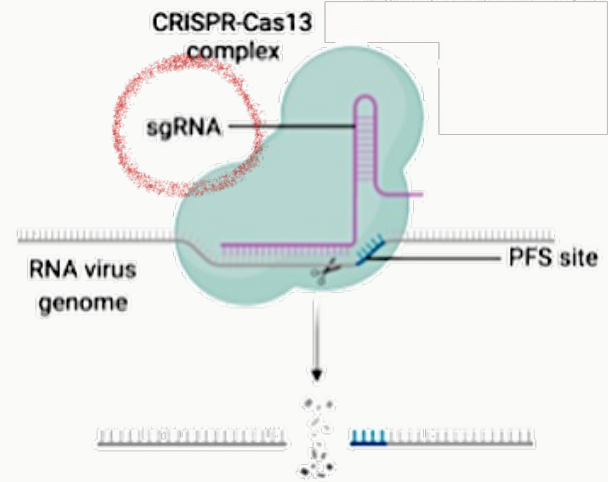
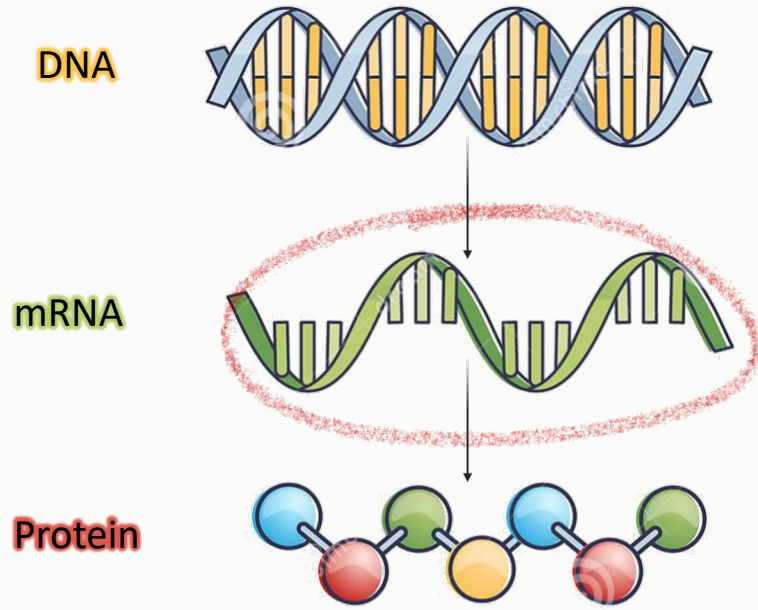
CRISPR/Cas13



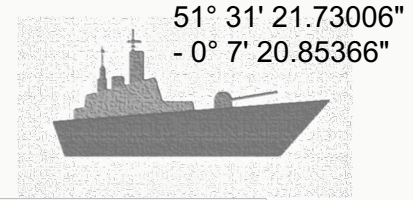
CIRTS
(CRISPR Inspired RNA Targeting System)



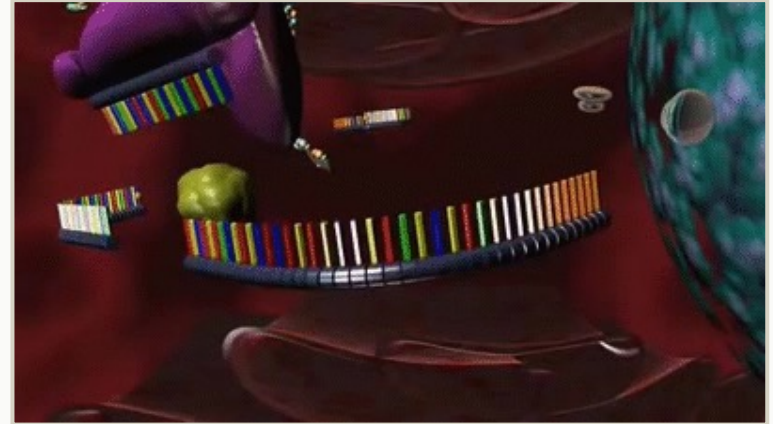
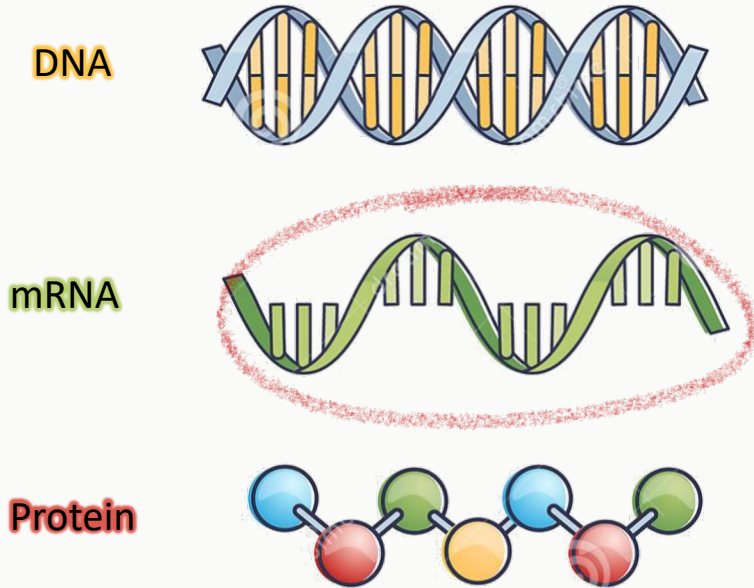
CRISPR/Cas13 – cleaving Androgen Receptor RNA using CRISPR



Degradation of RNA
[930 amino acids]

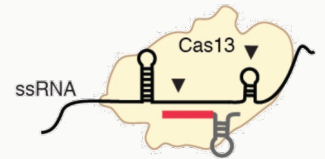
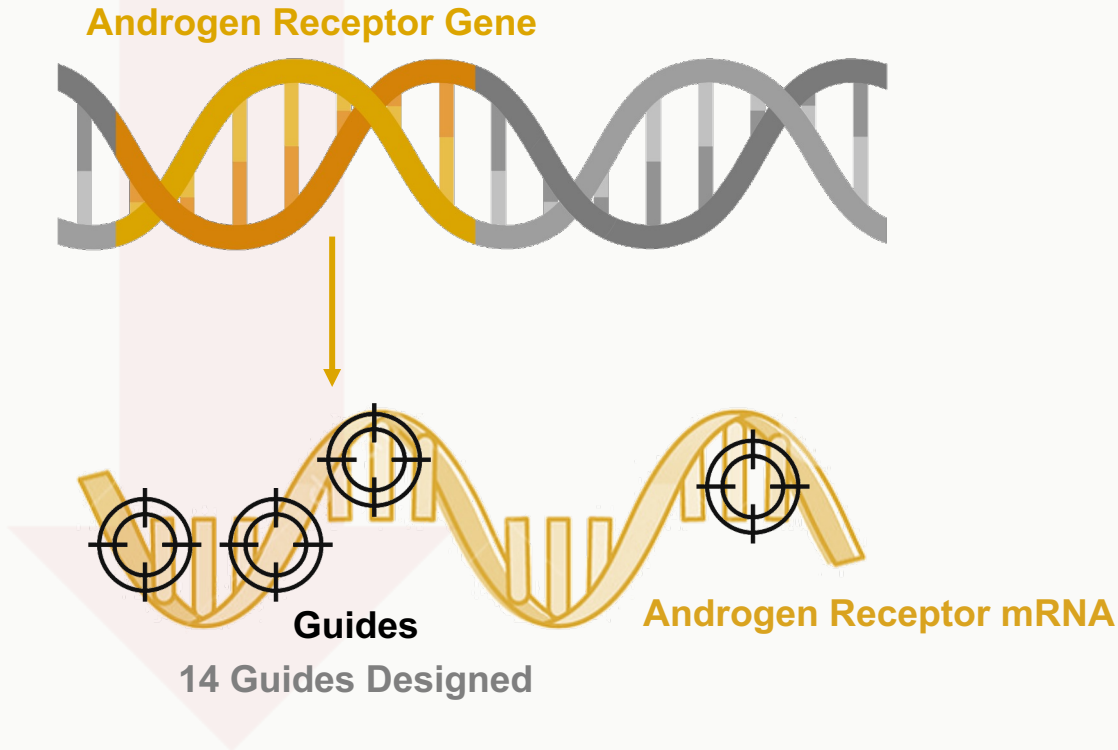


CRISPR/Cas13 – cleaving Androgen Receptor RNA using CRISPR

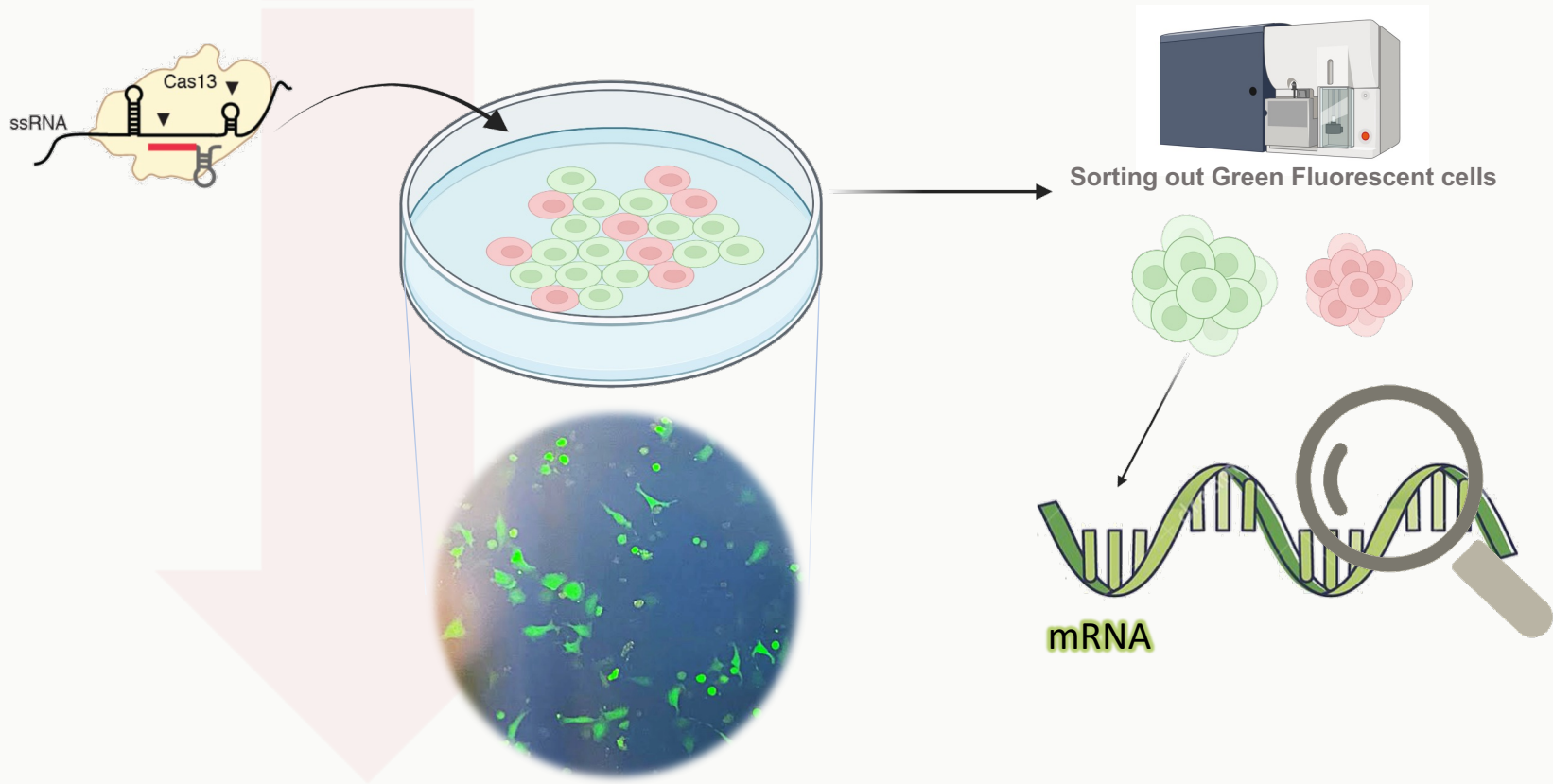


Degradation of RNA
[930 amino acids]

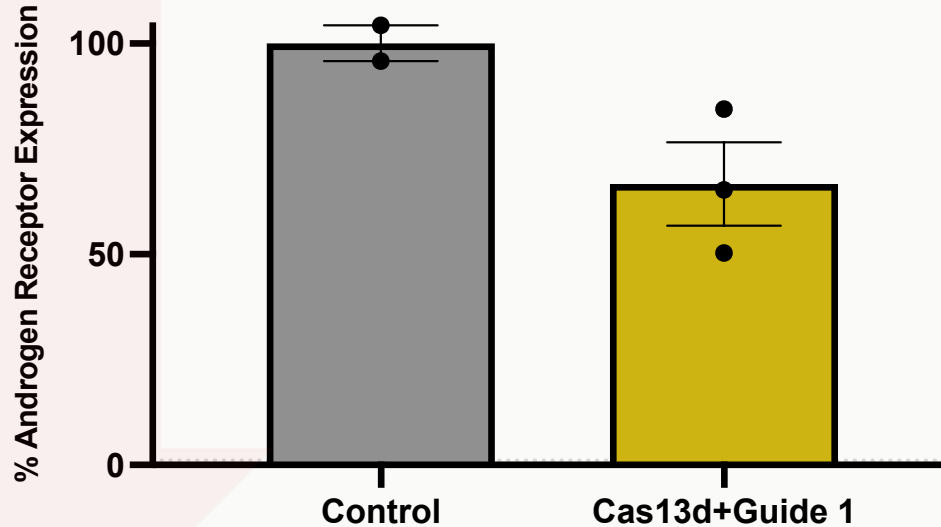
Designing Guides to target Cas13 to Androgen Receptor



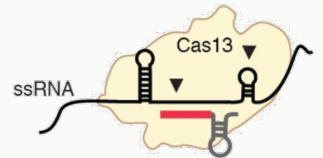
Testing Cas13 guides in human cells in culture



Expression of CRISPR/Cas13d shows promising reduction of AR expression

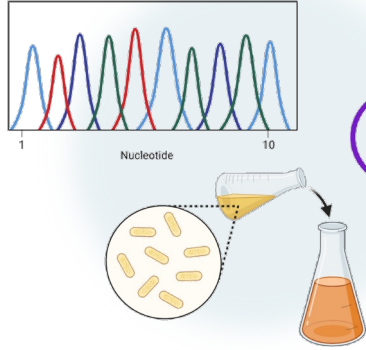


14 Guides Designed in total

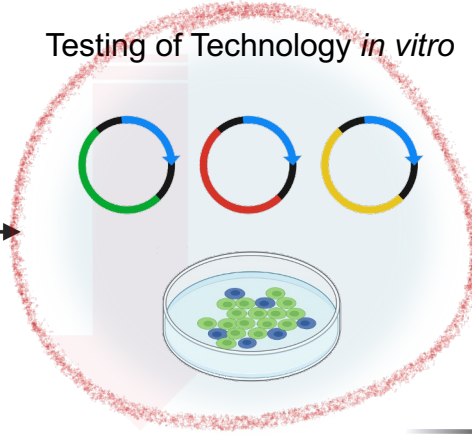


Overarching Plan of Project

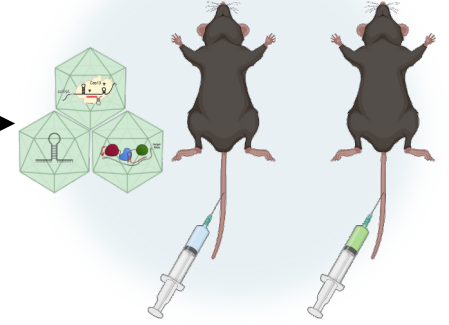
Design of AR Targeting Technology



Testing of Technology *in vitro*



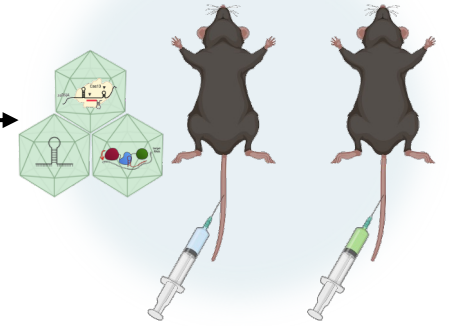
Delivery to Wild Type Mice



Investigating Strategies to Target Skeletal Muscle with AAV virus



Delivery to SBMA Mice



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