MYOTONIC DYSTROPHY FOUNDATION

Care and a Cure

2018

MDF ANNUAL CONFERENCE

September 14-15, 2018

Nashville, TN

INDUSTRY UPDATES ON DRUG DEVELOPMENT

Locana

Ranjan Batra, PhD VP, R&D

Locana is Committed to Development of Therapeutics for RNA-mediated Diseases

Company History

2016

- **Published Key Manuscript** (Nelles et al, *Cell)*
- **Incorporated Locana Inc** (Delaware C Corp)

2017

- **Published Key Manuscript** (Batra et al, *Cell)*
- **Licensed IP from University of California, San Diego**
- **Raised seed funding** (from 3 prominent institutional investors)
- **Initiated scientific operations at JLABS** (San Diego)

2018

- **Licensed additional IP from University of California, San Diego**
- **Locana selected for non-dilutive grant from Muscular Dystrophy Association**

Selected publications:

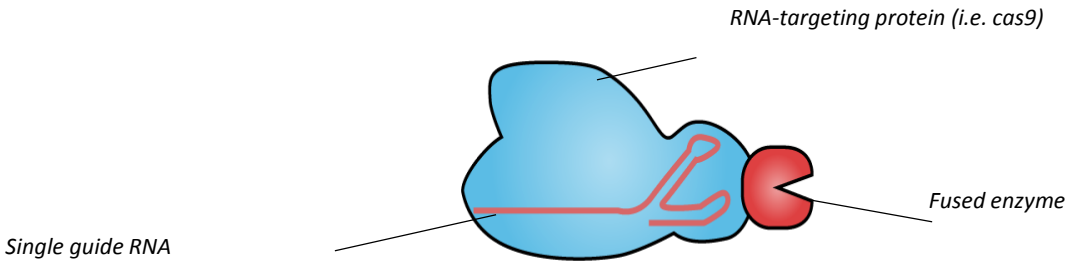
1) *Cell,* 2016, "Programmable RNA tracking in live cells with CRISPR/Cas9," Nelles, Yeo*, et al.*

2) *Cell,* 2017, "Elimination of Toxic Microsatellite Repeat Expansion RNA by RNA-Targeting Cas9," Batra, Nelles, Yeo, *et al.*

3) *Bioessays,* 2015, "Applications of Cas9 as an RNA-programmed RNA-binding protein," Nelles, Yeo, *et al.*

The Locana Platform

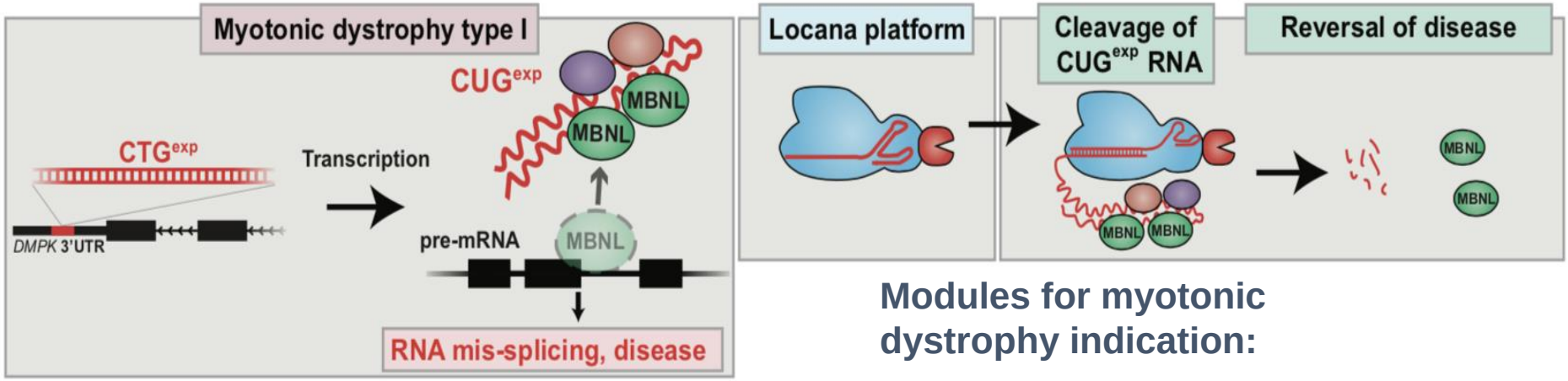
1. **Guide RNA (target specific)**
2. **CRISPR Effector, or comparable RNA-Targeting Protein – helps bind mutated RNA**
3. **Fused RNA-modifying enzyme – cleaves mutated RNA**



Locana's in-house screening assays rapidly link designs to therapeutic indications

With hundreds of single guide RNAs, RNA-targeting proteins, and fused enzymes, there are 1M+ possible chimeras that **each represent a potential therapeutics for genetic disease**

Loca-DMRX (RNA targeting CRISPR) binds to- and cleaves CUG-repeat containing RNA



Modules for myotonic dystrophy indication:

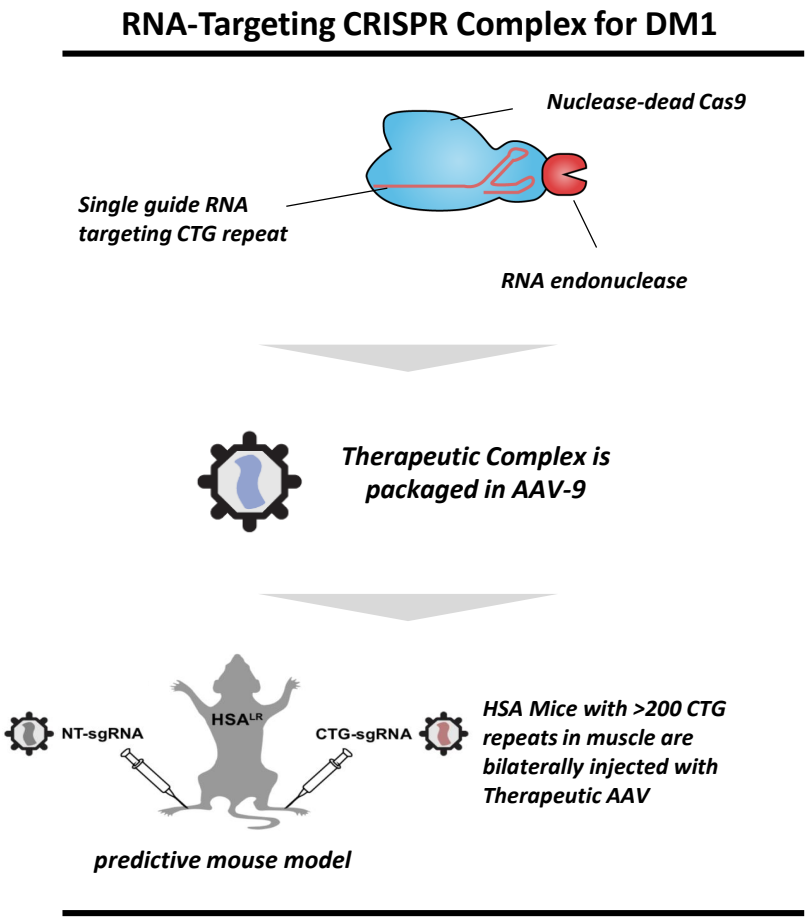
sgRNA: @CUG RNA

CRISPR protein: *S. pyogenes* Cas9

Enzyme: PIN endonuclease

Does RNA targeting CRISPR work in mice?

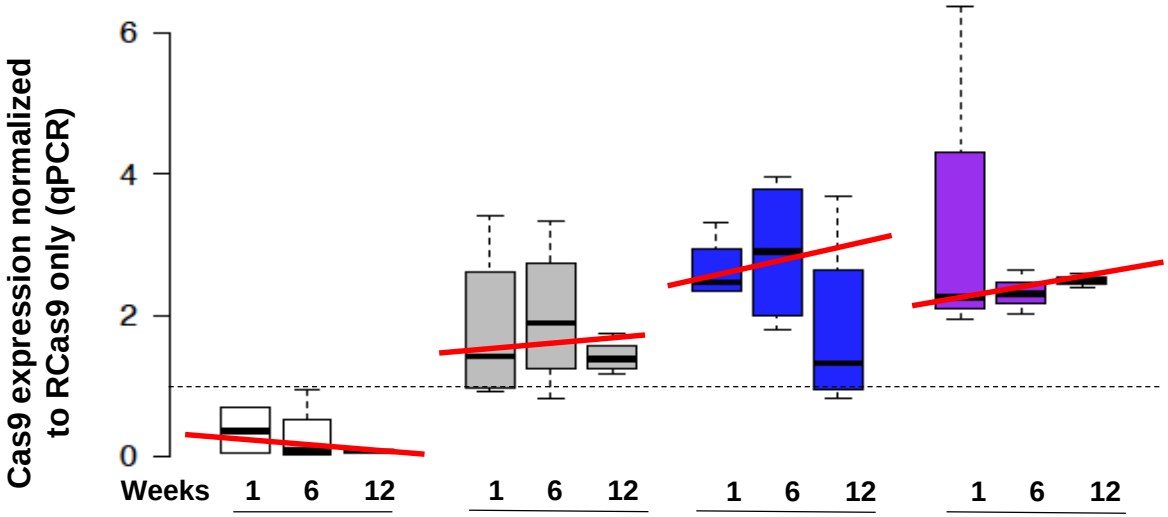
Approach:



Described in: "Reversal of molecular pathology by RNA-targeting Cas9 in a myotonic dystrophy mouse model," Batra, Nelles, Yeo et al. *BioRxiv* 2017.

RNA targeting CRISPR is Durably Expressed and safe in Muscle

Wildtype mice

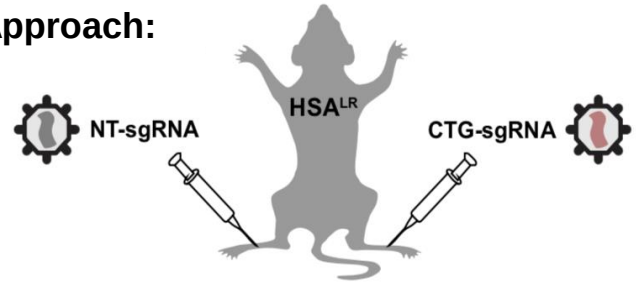


AAV9 RCas9				+			+			+	
AAV9 sgRNA		+		+			+			+	
Tacrolimus (s.c.)							+			+	
CTLA4 Ig (i.p.)										+	

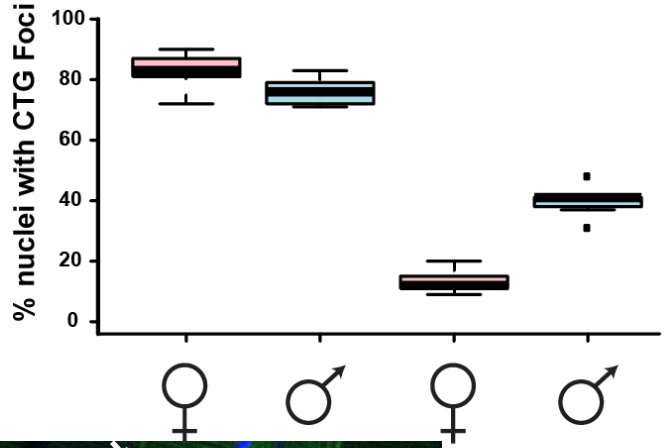
Robust, long term expression of RNA-targeting CRISPR even in the absence of immunosuppression

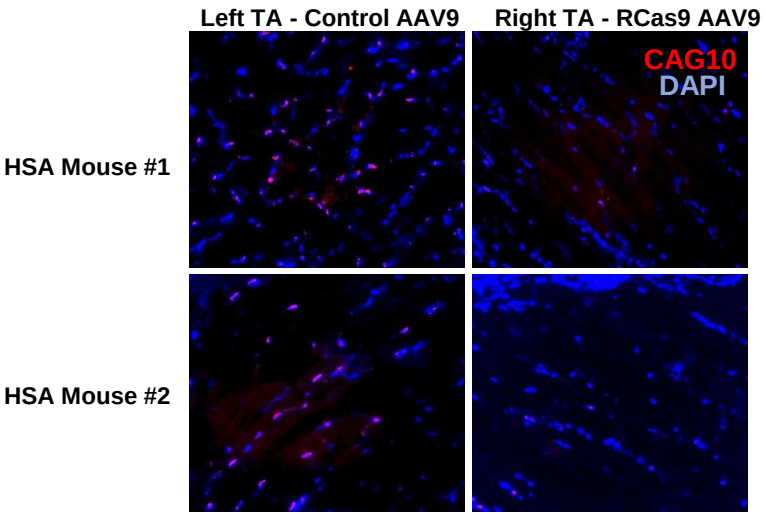
RNA targeting CRISPR – Reversal of DM1 *in vivo*

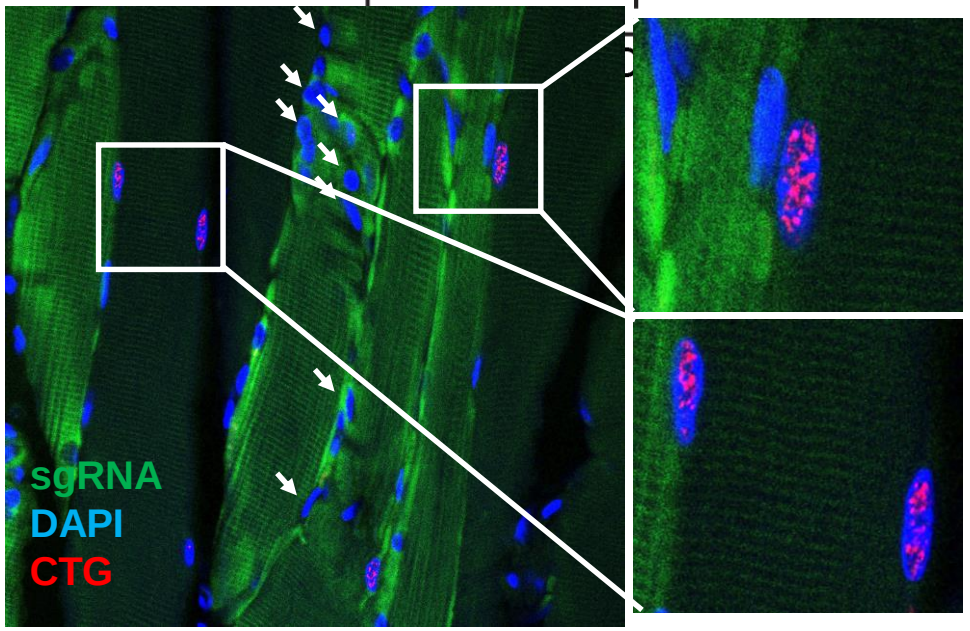
Approach:



Test 4 weeks post injection







Translation of Biologics and Small molecules to humans is hard!

Many Players in The Field

Exciting Time!

Tentative Timeline

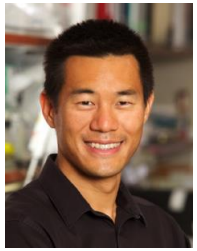
Route of Administration: **https://www.surveymonkey.com/r/HJRW5NJ**

Please take this 5 question Survey

We’re still figuring out our regulatory and Clinical Strategy and will provide an update soon!

We are Committed to Building a Gene Therapy for Myotonic Dystrophy

Gene Yeo, PhD MBA // Acting CSO/CEO

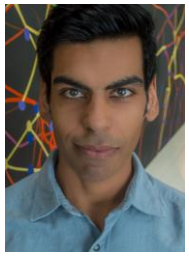


Co-founder and Professor of Cellular & Molecular Medicine, UCSD; Visiting Prof, NUS
Scientific strategy and academic/industry collaborations

Dave Nelles, PhD // CTO

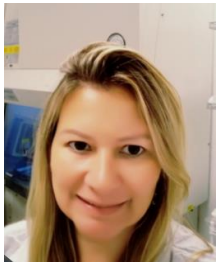
Yeo lab alum and co-founder; Developed RNA-targeting Cas9
Scientific strategy for product engine

Ron Batra, PhD // VP, R&D



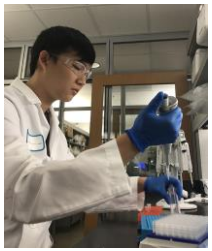
Yeo lab alum; Co-developed RNA-degradation of toxic RNAs
Scientific strategy for therapeutic delivery and preclinical studies

Daniela Martino Roth, PhD // Senior Scientist



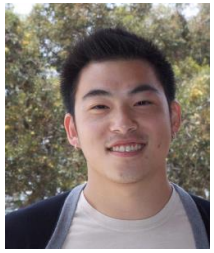
Experienced cell and molecular biologist.
Development of assays for product engine

Eric Byeon // Research Associate



Yeo lab alum; Experimental biologist.
Assays for product engine and preclinical studies

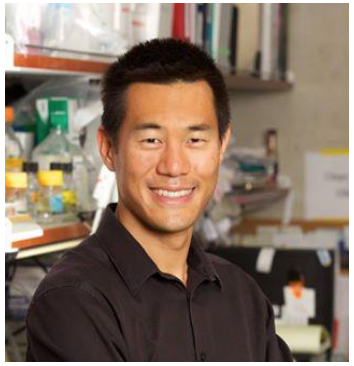
Patrick Liu, MS // Consultant, Bioinformatics



Yeo lab alum; Bioinformatics and machine learning.
CRISPR discovery

Locana

Special Thanks to Academic Collaborators and SAB members



Gene Yeo

#Yeolo Team

Steven Blue

Florian Krach

Maurice Swanson

Swanson Team

James Thomas

Curtis Nutter

Lukasz Schneider

Neurosurgeon with international leadership in the delivery of biologics to the spinal cord

Martin Marsala, MD, UCSD

Marsala Team

Takadoro Takahiro - Anesthesiologist

Oleksander Platoshyn – EMG scientist