Therapeutic restoration of muscle regeneration in Duchenne

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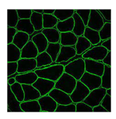
Acknowledgments
Duchenne (Mdx) program data: OHRI, Rudnicki Lab, Satellos workgroup

Our Company

Imagine a simple pill than can re-initiate the physiological process which enables muscle fibers to repair and regenerate. Satellos is a biotechnology company founded on game changing science in skeletal muscle regeneration. We have discovered that muscle stem cells in Duchenne are unable to adequately repair existing, and generate new, muscle fibers throughout life. We believe this is an even more significant factor in the progressive muscle damage experienced by people living with Duchenne than the absence of the dystrophin protein in existing muscle fibers. This is because dystrophin has an earlier role to play in creating muscle progenitor cells which ultimately repair and regenerate muscle fibers. We have identified multiple ways, including through master regulators, to correct this stem cell deficiency with small molecule drugs through regulation of a process known as stem cell "polarity". Our approach has potential to be disease modifying in Duchenne and other dystrophies as detailed in this poster.

Dystrophin's duality: a role for regeneration

What we know:
Dystrophin in fibers provides structure



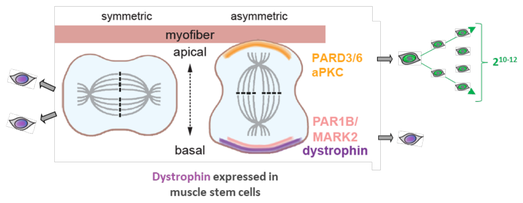
Dystrophin expressed in muscle fibers

SOLID BIOSCIENCES · SAREPTA THERAPEUTICS · Pfizer

Proposed solution: genetic therapies to restore dystrophin protein in fibers

NS Pharma · Dyne · AVIDITY BIOSCIENCES · PepGen

Satellos discovery:
Dystrophin in stem cells drives regeneration



Dystrophin expressed in muscle stem cells

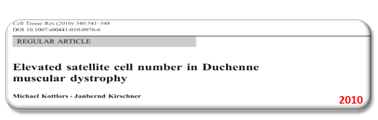
Satellos solution: reset polarity in stem cells to rescue regeneration

Muscle progenitor cell · Muscle stem cell

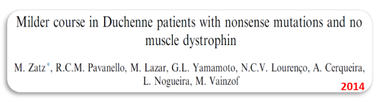
Image adapted from Flanigan et al. 2021 MedRxiv

Figure 1. Satellos discovered that the dystrophin protein participates in establishing muscle stem cell polarity. Polarization drives the regeneration process by instructing each stem cell to create a muscle cell progenitor which enables the repair/generation of muscle fibers. In essence, Duchenne is a disease of failed regeneration, offering the potential for an entirely new treatment approach.

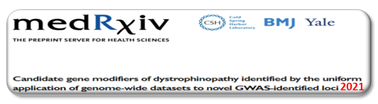
Evidence of the problem and support for the solution



- Clinicians observe elevated stem cells in Duchenne patients
- Supports thesis of polarity and regeneration deficit
- Significance not understood at the time



- Dystrophin null escaper Duchenne families identified
- Functional muscle possible absent dystrophin
- Enhanced regeneration via Notch3 mutation*



- Retrospective analysis of patients who walk 20+ years
- Polarity/regeneration inducing SNP implicated
- Rudnicki work cited extensively

* https://youtu.be/Rfobvyo6EzU?t=2365 – Study update from Dr. Lou Kunkel

Three tier discovery-to-POC screening platform

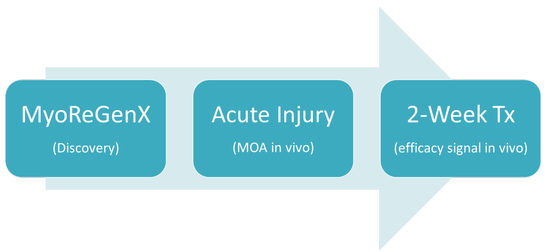


Figure 3. Satellos' proprietary screening platform supports in house drug development from target discovery through to POC efficacy studies in preclinical mouse models of Duchenne.

MyoReGenX™: novel stem cell polarity screen

K9 is a proposed regulator of Notch signaling

Figure 4. MyoReGenX™ is an in-niche screening platform that evaluates muscle stem cell divisions as they take place on in-tact muscle fibers. MyoReGenX™ has unveiled a number of targets and pathways capable of regulating muscle stem cell polarity and regeneration. Satellos has prioritized a kinase target codenamed "K9" as a potent modulator of asymmetric division and progenitor restoration from Duchenne muscle stem cells.

"K9" an appealing, druggable target

- ☑ Modulates proposed MOA – *genetic and small molecule in house data*
- ☑ Druggable Class – *currently under active development in unrelated indication*
- ☑ Clinical Safety – *hundreds of patients dosed across PhI & PhII studies with no drug SAEs*
- ☑ Safe Chemophores - *fast follower strategy rapidly put in place yielding best in class molecules*

Enablement of a rapid K9 drug development program

Rapid development of fast follower chemistry program

SERIES A → **Lead Compound Series**

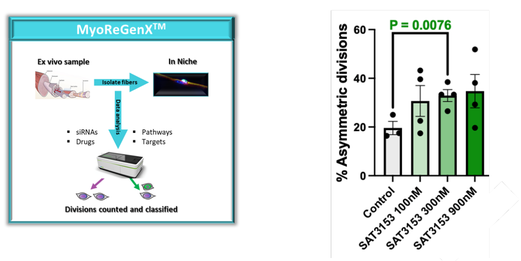
- Nanomolar potency
- Kinome selectivity
- PK, ADME, hERG all acceptable

SERIES B/C → **Back-up/Second Compound Series**

- Enhanced potency
- Advanced SAR/optimization ongoing
- Compounds moving to ADME/PK

Nomination of SAT-3153 as pre-IND lead compound

SAT-3153 restores polarity and asymmetric divisions



SAT-3153 is potent regulation of asymmetric divisions

Figure 4. SAT-3153 restores polarity in Duchenne muscle stem cells, driving asymmetric division and restoring progenitor formation in isolated myofibers. N=4 individual wells of myofibers per condition measured for asymmetric division via MyoReGenX™.

SAT-3153 restores asymmetric division in vivo

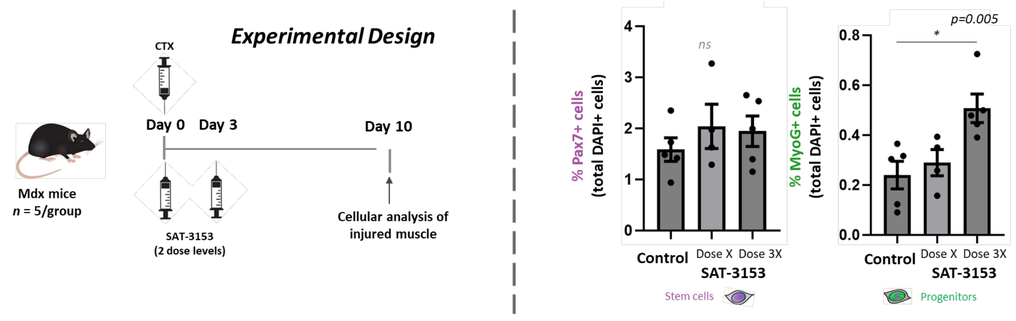


Figure 4. Systemically delivered SAT-3153 restores polarity in Duchenne muscle stem cells, driving asymmetric division and restoring progenitor formation in Mdx mice. N=5 mice per group. Cardiotoxin injured TA muscles were collected, processed and single cells collected for immunocytochemical analysis for Pax7 and MyoG. IP route of administration.

SAT-3153 improves muscle force

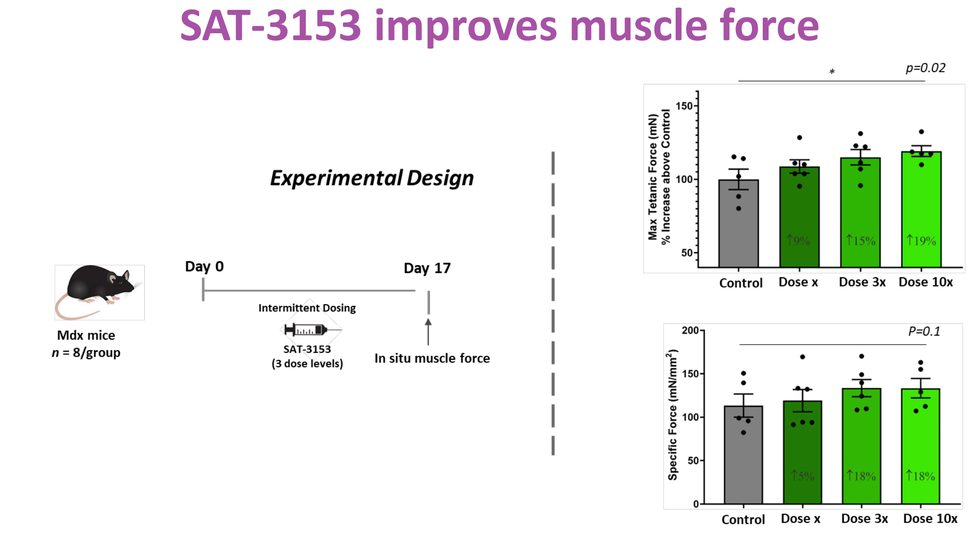


Figure 4. Repeat dosing of SAT-3153 over two weeks is sufficient to improve TA muscle force in Mdx mice. N=8 mice per group. In situ muscle force was measured using Aurora Scientific physiology system. IP route of administration.

Summary & Next Steps

Satellos is endeavoring to develop the first ever small molecule therapeutics expressly targeting muscle stem cell polarity as a novel treatment modality for Duchenne, and potentially other degenerative muscle diseases. We plan to progress SAT-3153 through additional preclinical efficacy studies in preparation for evaluation across a full package of IND enabling studies scheduled for H2 2023. Our goal is to be clinic ready by end of year/early 2024.