Significantly enhanced muscle tropism with reduced liver biodistribution at low doses using an optimized AAVrh74-based capsid in NHP

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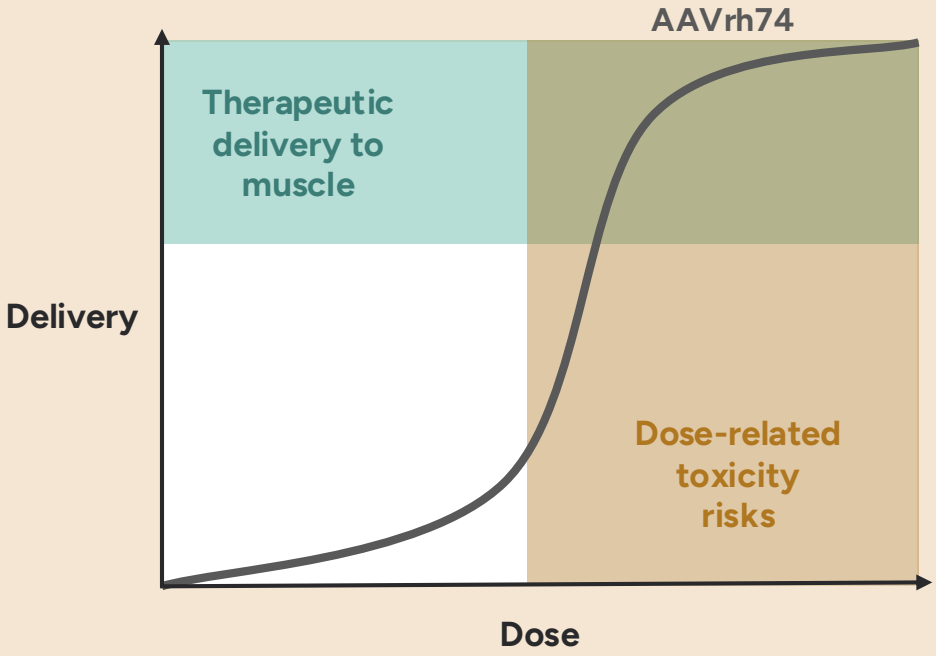
Disclosures

I am a full-time employee of Dyno Therapeutics®

Gene therapy for DMD: efficacy at a cost

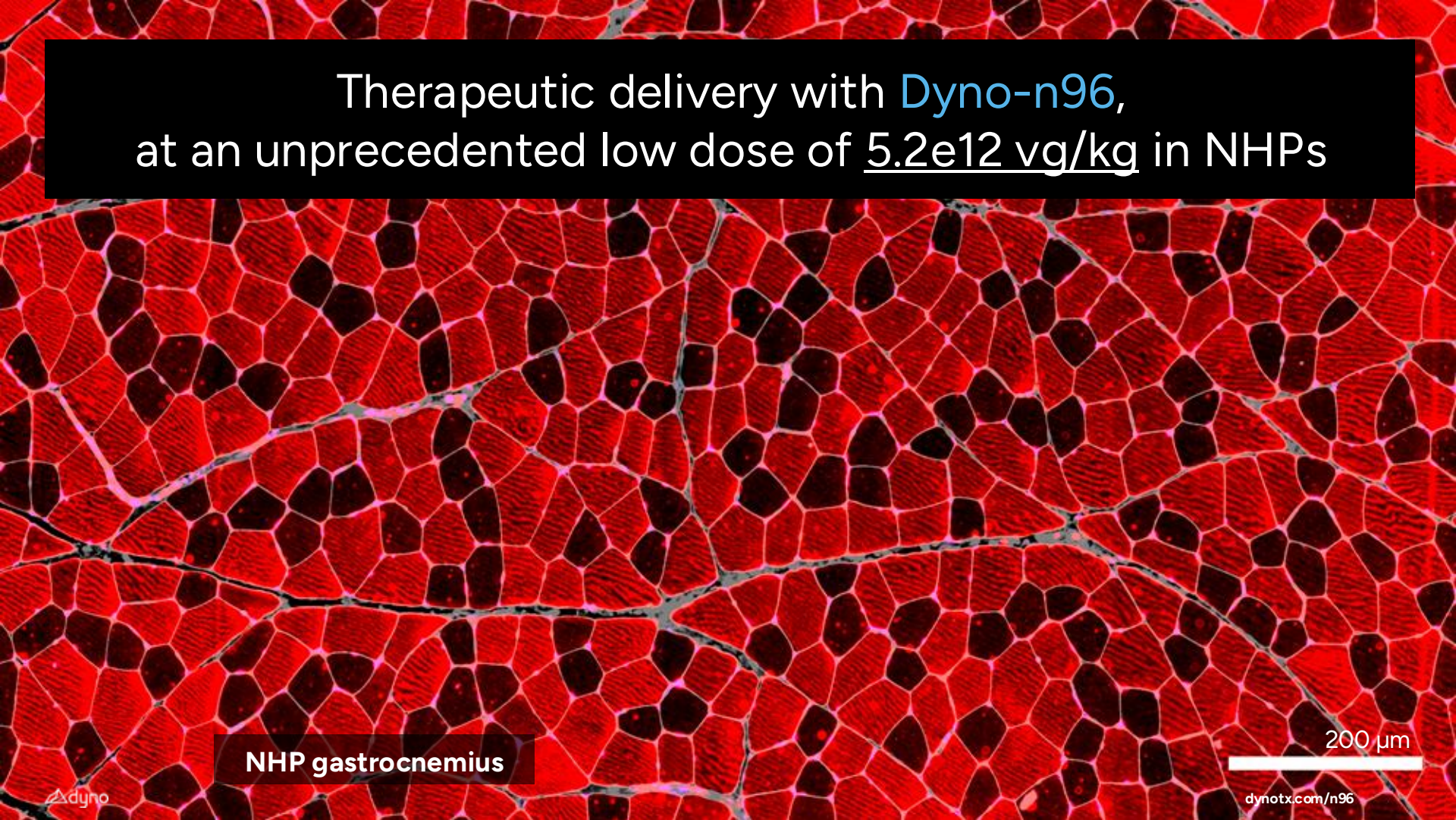
ELEVIDYS, the only FDA-approved gene therapy for muscular dystrophies, is an AAVrh74-based gene therapy that requires a high systemic dose of 1.33e14 vg/kg to reach efficacy



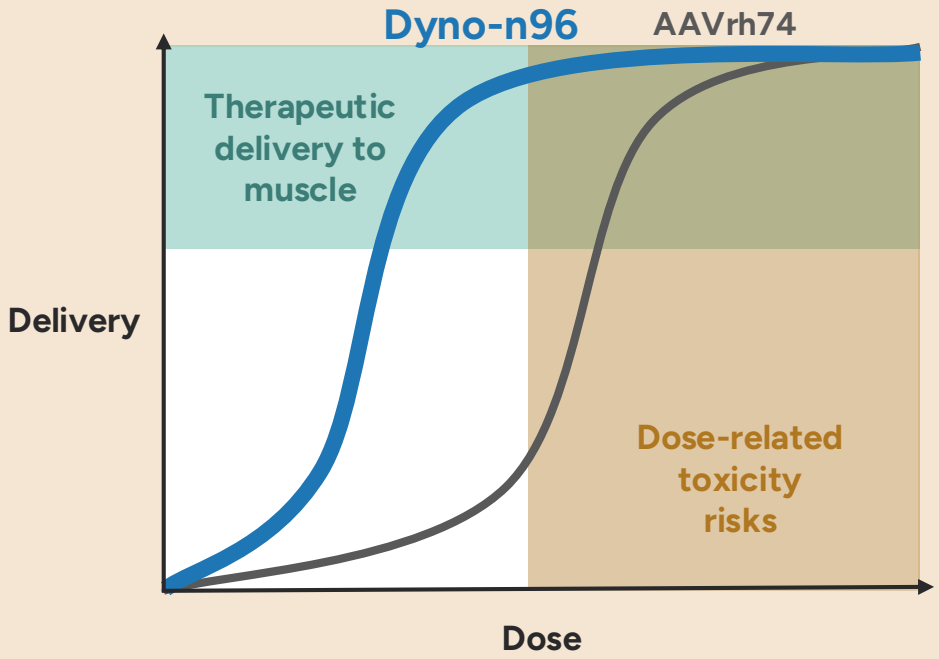
The capsids we need

- Safer
- More effective
- Cheaper

Therapeutic delivery with Dyno-n96, at an unprecedented low dose of 5.2e12 vg/kg in NHPs



AI-designed Dyno-n96 achieves therapeutic delivery at a low dose, improving safety and reducing costs



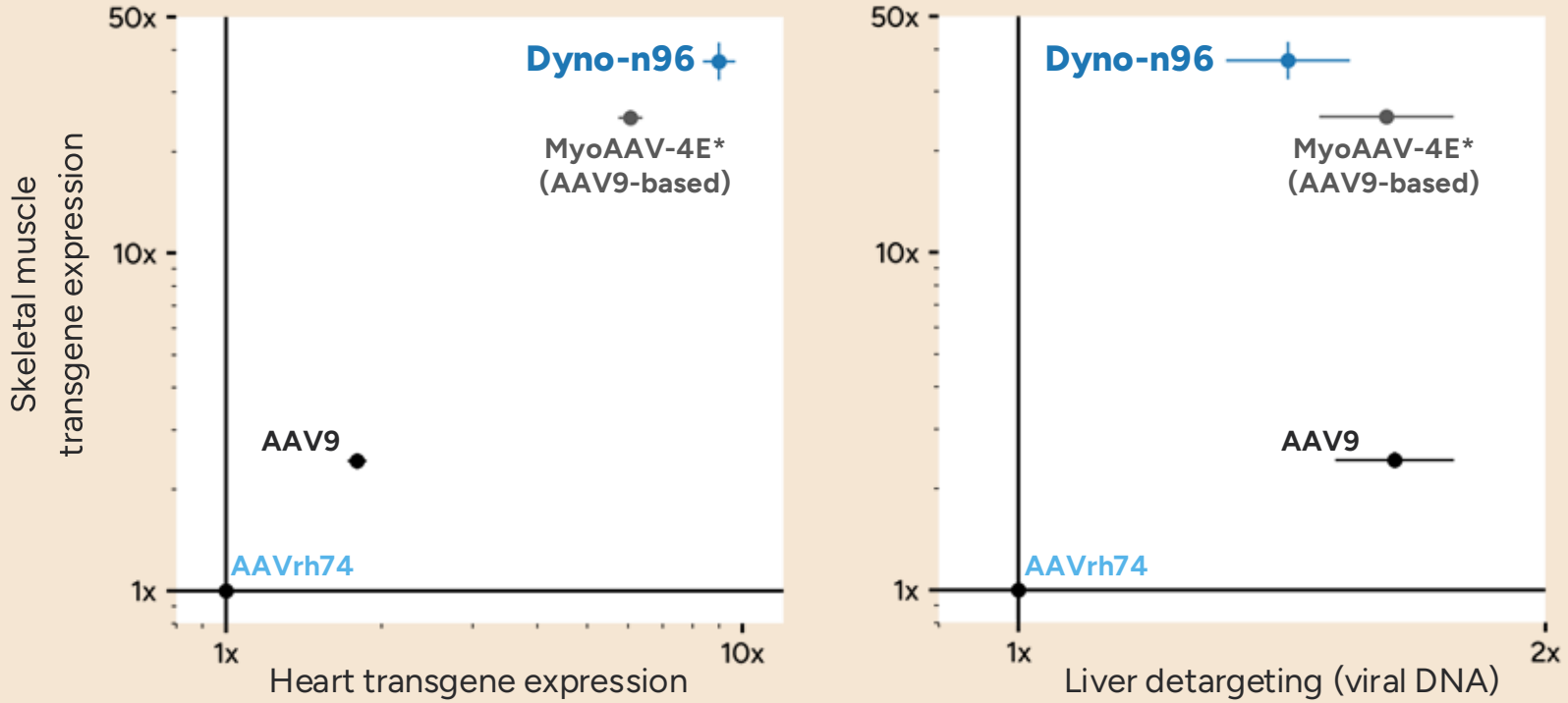
Dyno-n96

- Safer
- More effective
- Cheaper

Dyno's AI models are serotype agnostic, capable of designing new capsids that are better than any previously tested capsid

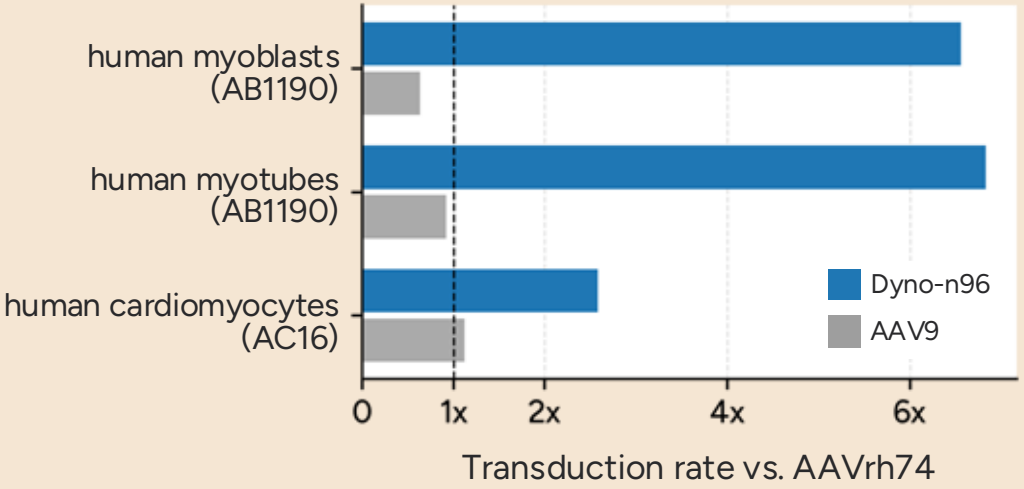
Optimized design of Dyno-n96 enables targeting skeletal muscle and heart while detargeting liver in NHP vs AAVrh74

Data from small, pooled capsid study in NHPs



*MyoAAV-4E, Tabebordbar et al. 2021. *Cell*

Dyno-n96 has a high likelihood of human translatability based on performance in relevant human cell lines



Dyno-n96 was externally produced at scale to enable our NHP validation study

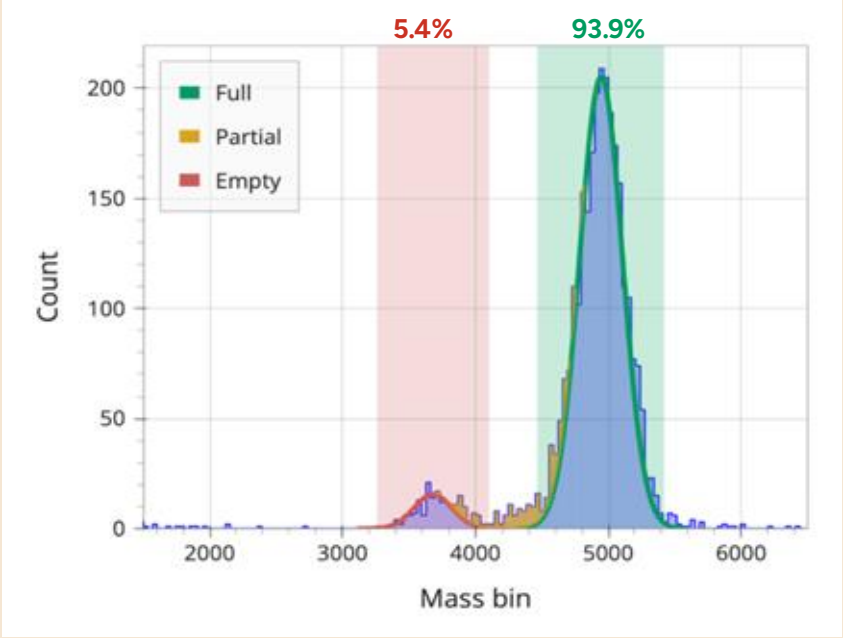
Dyno-n96 is easy to produce

- Similar to AAVrh74 and AAV9

Dyno-n96 production and purification is scalable

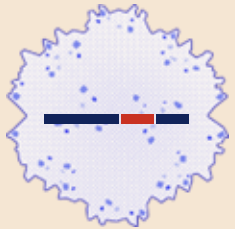
- Manufactured via suspension bioreactor
- Purified with affinity and ion exchange chromatography
- Mass photometry confirms high quality results

Refeyn Mass Photometry

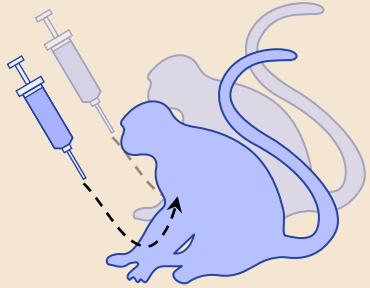


Aggregate of at least 4 replicate acquisitions (Trisk data)

We compared Dyno-n96 head-to-head in NHPs with a published capsid, MyoAAV-4E*



Dyno-n96 capsid
packaging CBh-**mCherry**
genome with ssAAV ITRs

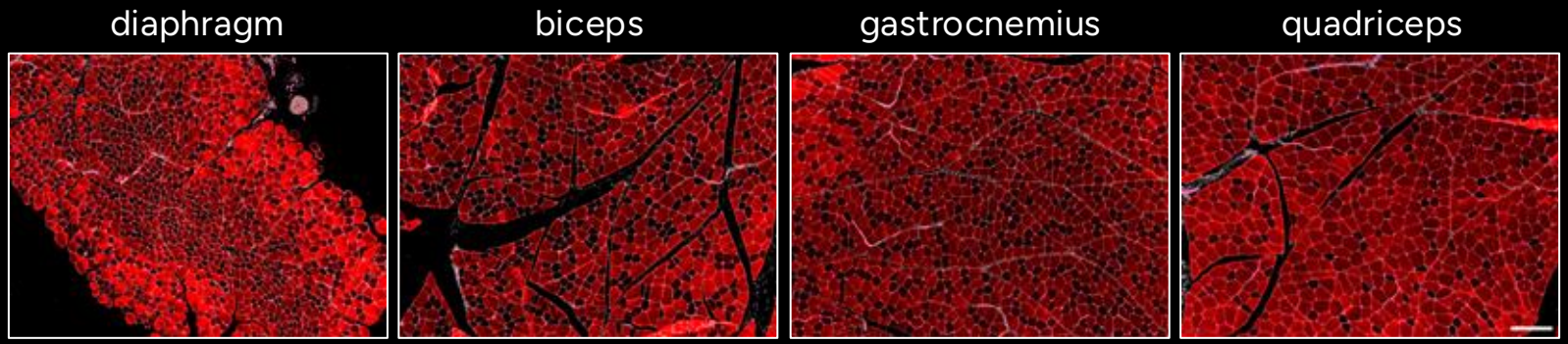


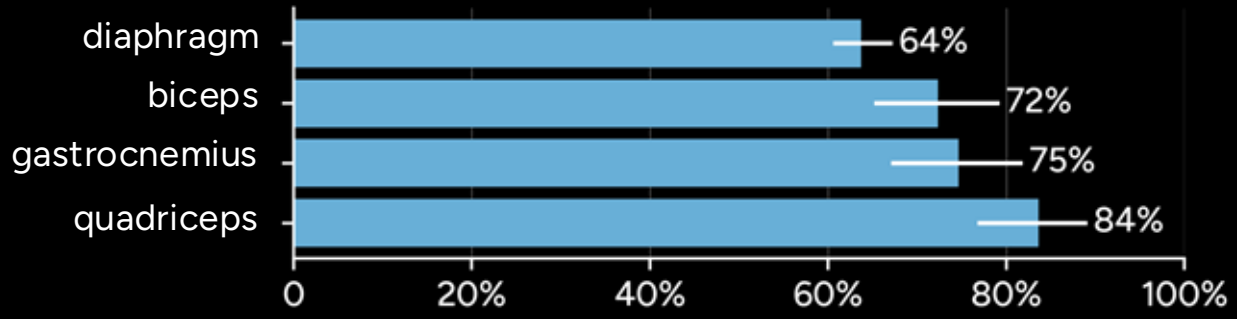
2 Adult Cyno NHPs
5.2e12 vg/kg
28 days in life

5.2e12 vg/kg is 25x lower than Elevidys (1.33e14 vg/kg)

*MyoAAV-4E, Tabebordbar et al. 2021. *Cell*

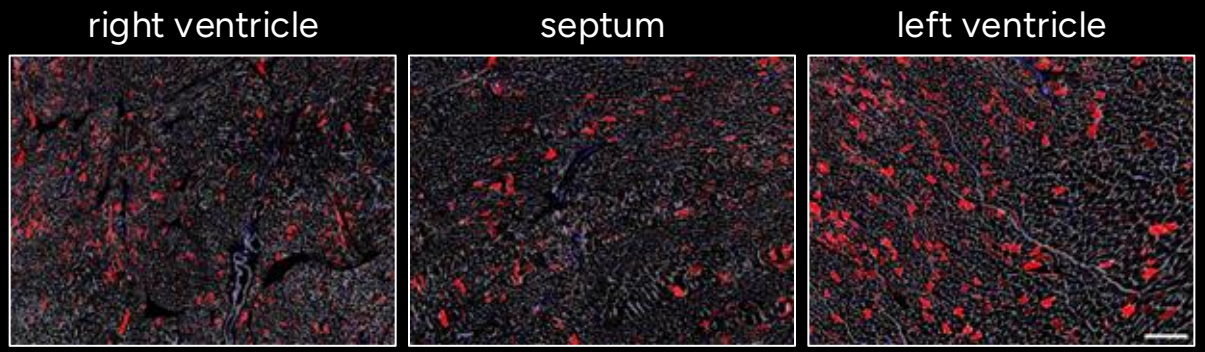
At 5.2e12 vg/kg, Dyno-n96 evenly transduces an average of 74% of skeletal myofibers across several tissues

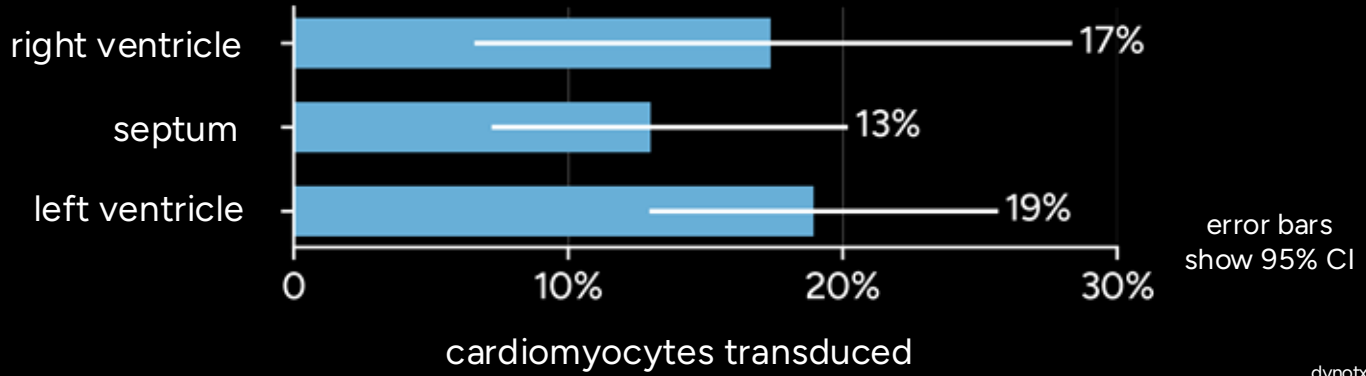




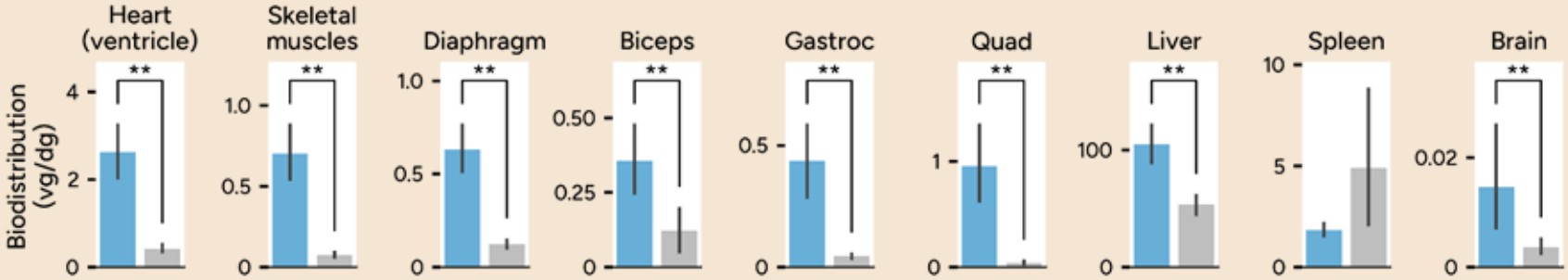
error bars show 95% CI

At 5.2e12 vg/kg, Dyno-n96 delivery to ventricular cardiomyocytes remains efficient





Dyno-n96 more potent than MyoAAV-4E in muscle and heart



Dyno-n96, 5.2e12 vg/kg

MyoAAV-4E, 5.2e12 vg/kg

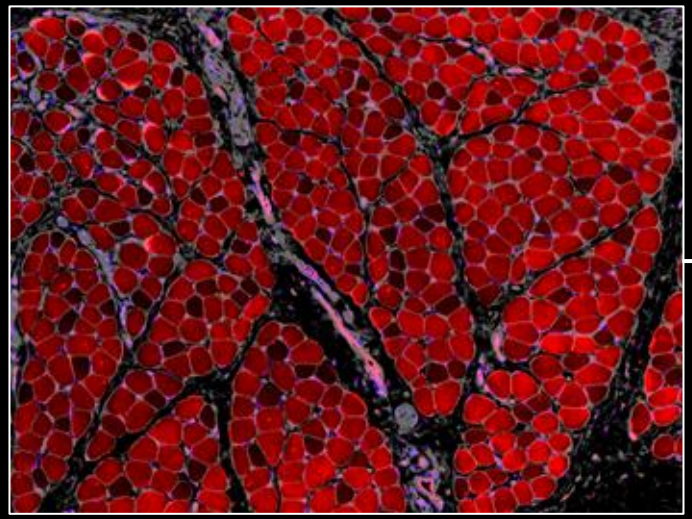
Error bars show 95% CI

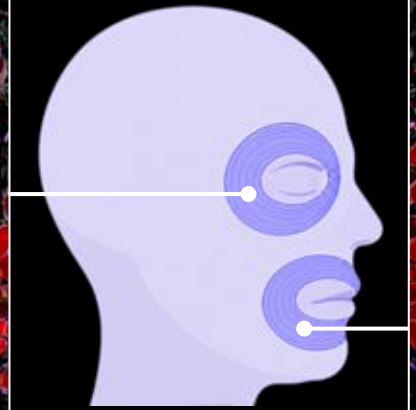
* p < 0.05

** p < 0.01

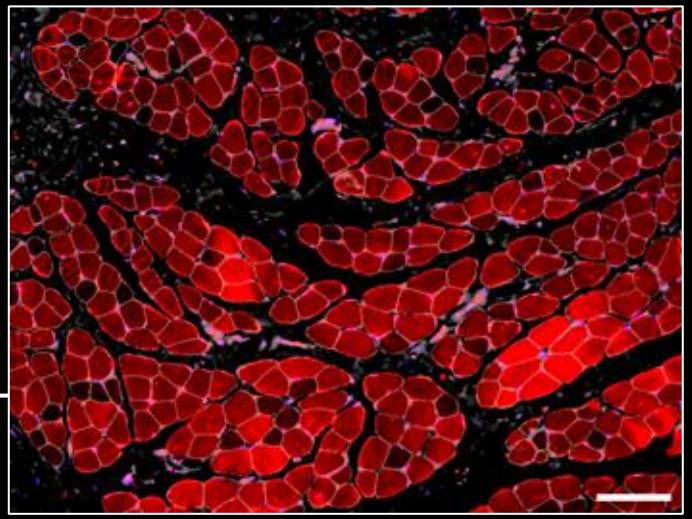
At 5.2e12 vg/kg, Dyno-n96 delivers efficiently to facial muscles in NHP, key targets for disorders such as FSHD

orbicularis oculi





orbicularis oris



WGA, mCherry (Dyno-n96), DAPI

Scale = 100 µm

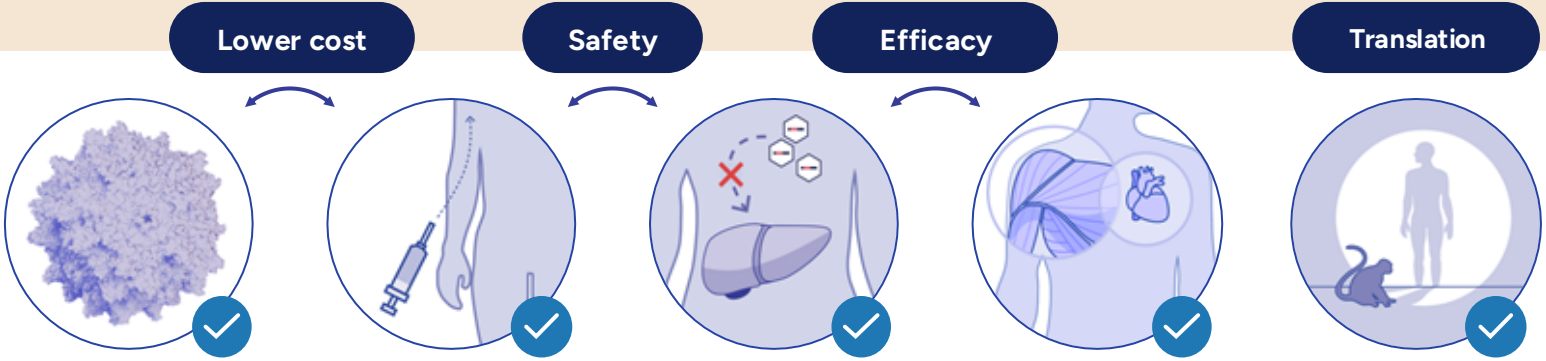
Dyno-n96 transduces around 50% of satellite cells, positioning it as a promising candidate for gene editing applications

WGA, PAX7, mCherry (Dyno-n96), DAPI

5.2e12 vg/kg IV

Scale = 10 µm

Dyno-n96 achieves therapeutic delivery to muscle at significantly lower doses and with improved liver detargeting



Efficient production

similar production vs AAV9

Efficient at low doses

5.2e12vg/kg

Detargeted from liver

1.4x < AAVrh74 in liver

Targeted delivery to multiple organs

74% avg muscle
16% avg heart
at 5.2e12vg/kg

Predict performance in humans

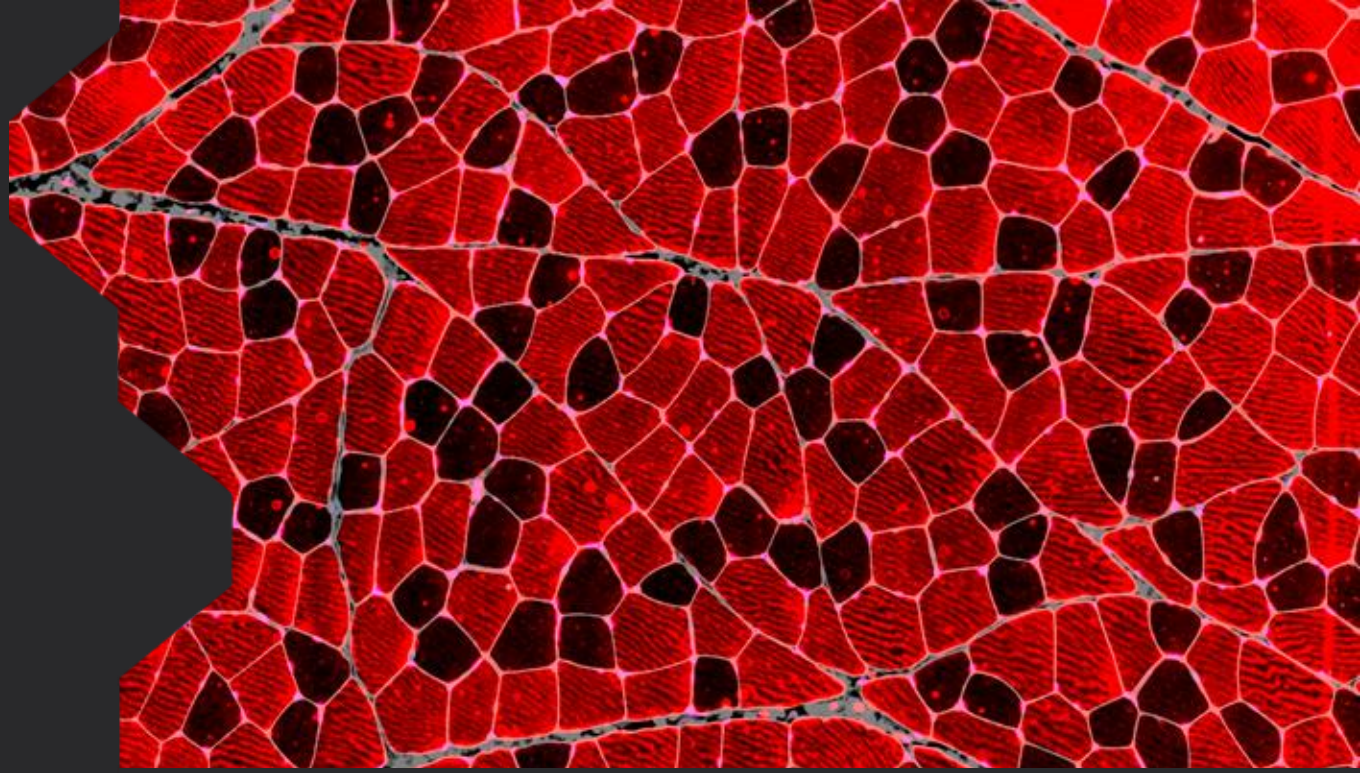
Enhanced transduction in relevant human cell lines

dyno

DYNO FRONTIERS NETWORK

Access Dyno capsids.

EASY.



More from Dyno at ASGCT

- #1042 & 1043 Poster Session (CNS); May 12
- **#172 AAV Capsid Eng. II (Muscle); May 13**
- Dyno Symposium; May 13
- Advancements in AAV and lentivirus vectors; May 14
- Bio-Techne - RNAscope Profiling of AI-designed AAV Capsids; May 14