



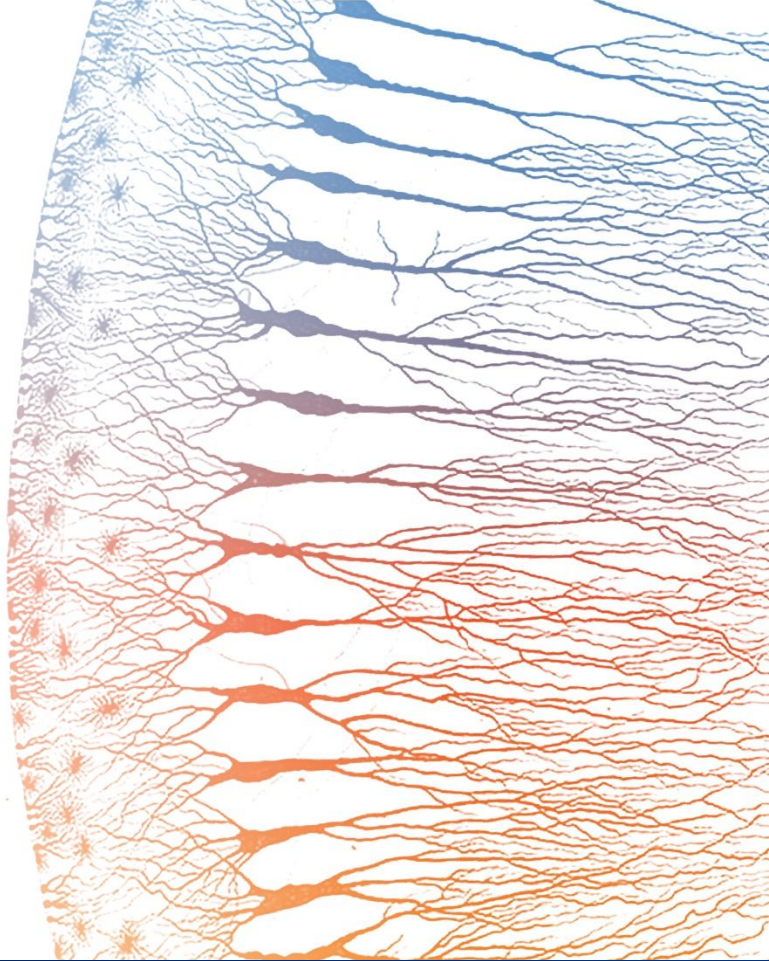
Directed evolution of muscular and neuromuscular capsid variants in both mice and non-human primates (#422)

Tyler Moyer

ASGCT 2026 Annual Meeting

AAV Capsid Engineering IV

Friday, May 15, 2026



Tyler Moyer is a full-time employee of Voyager Therapeutics, Inc.

- Voyager's TRACER™ engineering platform focuses on evolving AAV capsids with tissue-specific targeting for maximal gene delivery and minimum off-target effect upon systemic delivery.
- TRACER™ was first applied to deliver transformative, BBB-penetrant AAV vectors for CNS-specific gene delivery.
- Given the continued need for improved AAV capsids across therapeutic areas, the TRACER™ platform is now leveraged to engineer capsids with non-CNS specificity and dual-tissue tropism.

Presentation ID 163

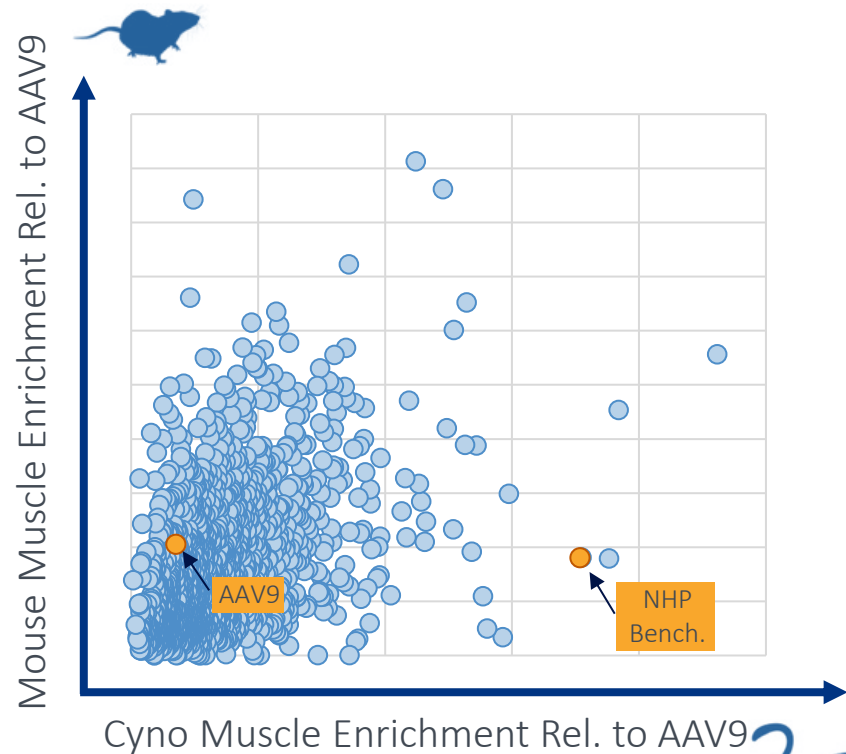
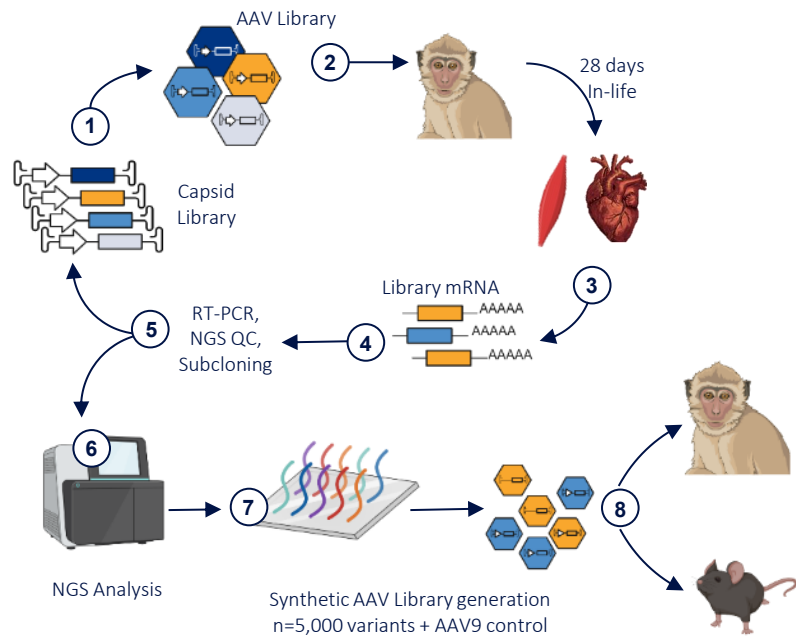
Title: Intravenous Delivery of VY1706, a CNS Penetrant AAV Gene Therapy for Alzheimer's Disease, Demonstrates Compelling Pharmacology and Safety in a 3-Month GLP Toxicology Study in NHPs

Presenter: Todd Carter, CSO

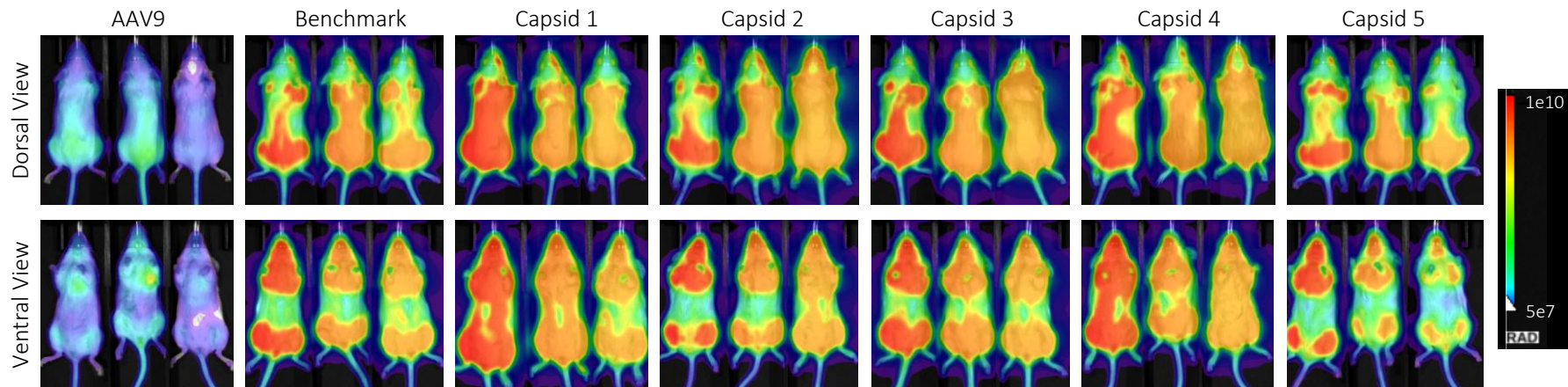
Late Breaking Abstracts; Wednesday, May 13, 8:30 AM

AAV Directed Evolution Platforms (TRACER) Can Be Used to Evolve Tissue-Specific AAV Variants

- TRACER (Tropism Redirection of AAV by Cell-type specific Expression of RNA) evolution of peptide libraries



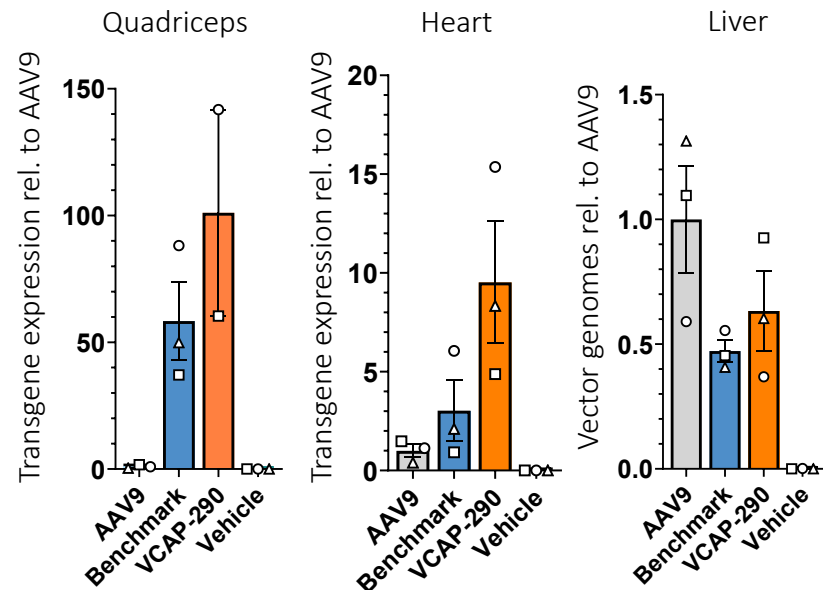
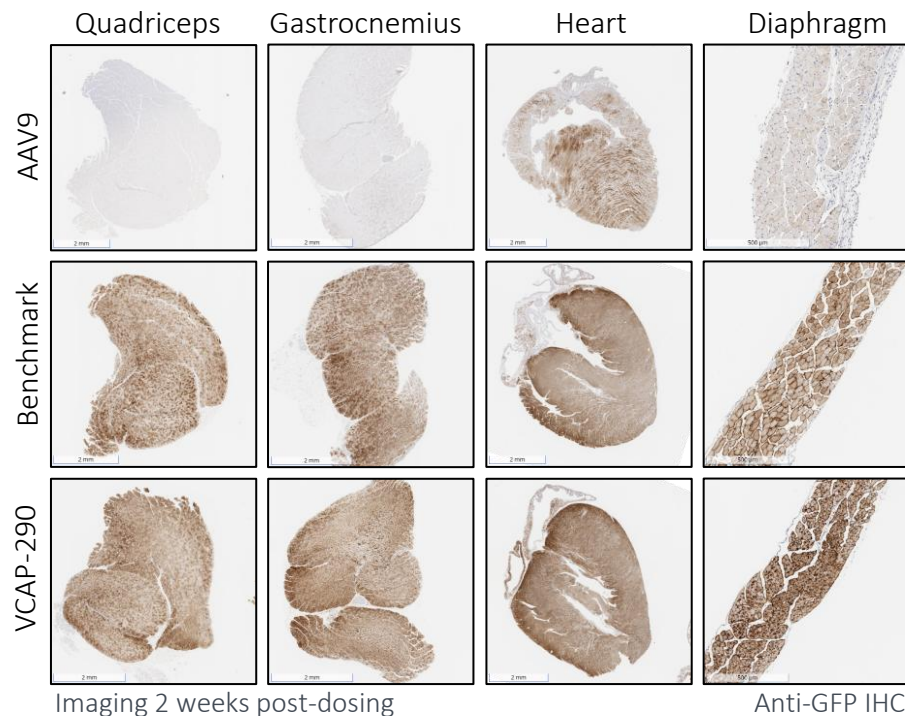
TRACER™-Derived Muscle Capsids Demonstrate Superior Muscle Transduction Over AAV9 in Mice



Imaging 2 weeks post-dosing

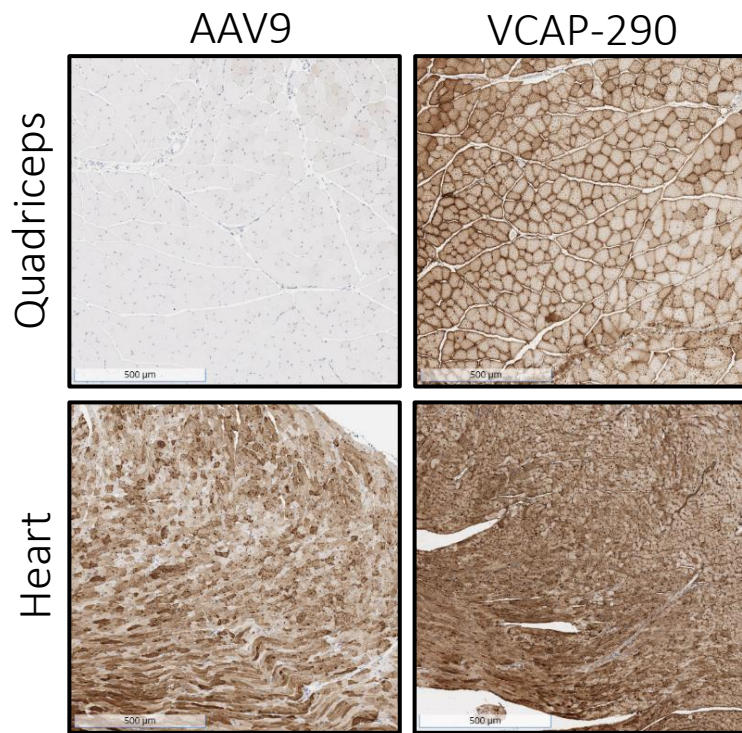
6-8 week old female B6(cg)-Tyrc-2J/J mice IV-dosed with 2.5E13 VG/kg of capsid packaged with ssCAG-EGFP-T2A-Luciferase transgene

VCAP-290 Demonstrates Superior Muscle Transduction Over AAV9 in Mice

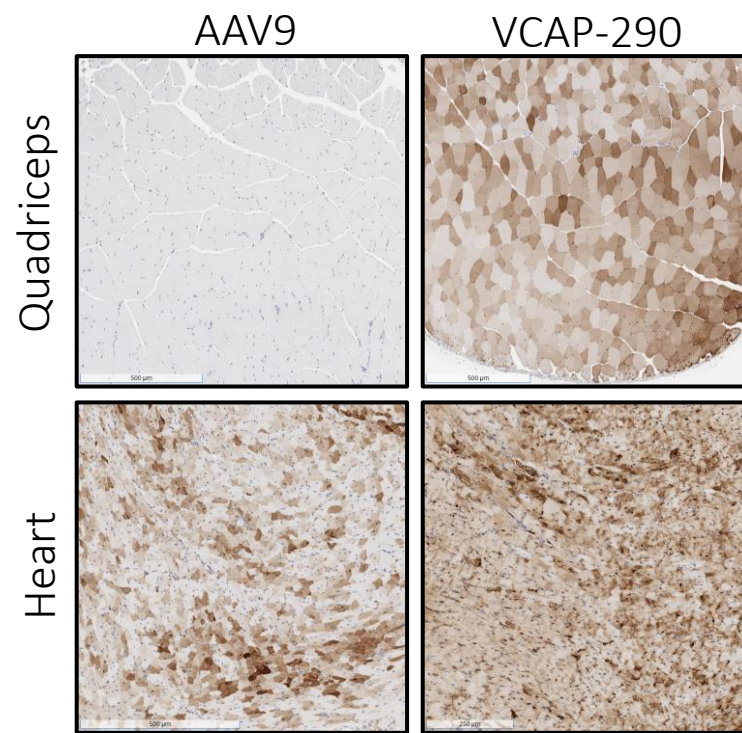


6-8 week old female B6(cg)-Tyrc-2J/J mice IV-dosed with 2.5E13 VG/kg of capsid packaged with ssCAG-EGFP-T2A-Luciferase transgene

VCAP-290 Transduces 100% of Muscle Fibers at 5E12 VG/kg in Mice

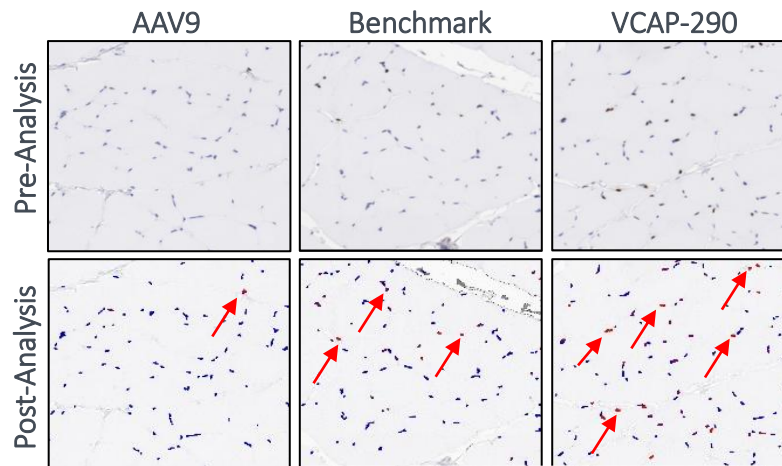
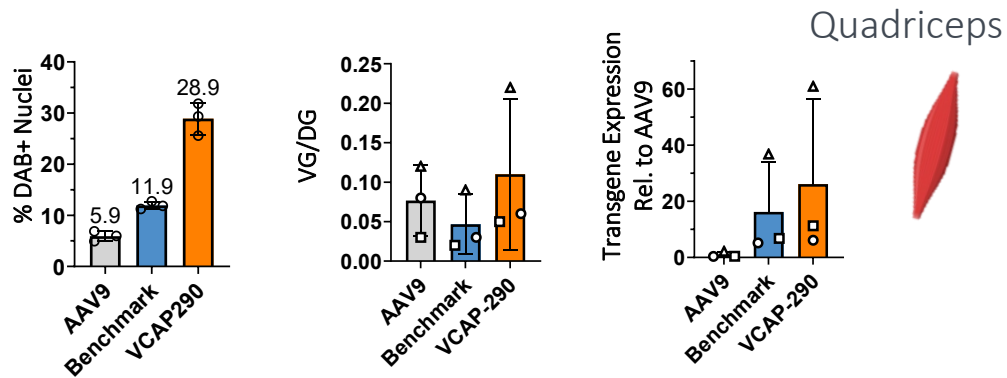
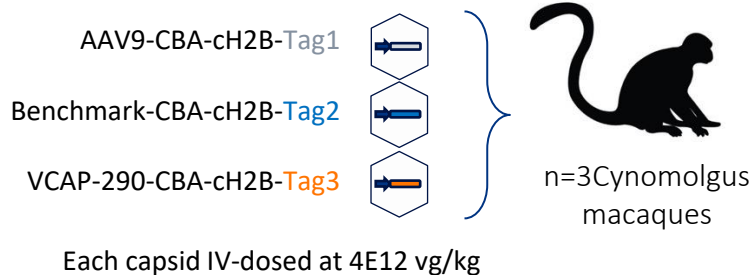


6-8 week old female B6(cg)-Tyrc-2J/J mice IV-dosed with 2.5E13 VG/kg of capsid packaged with ssCAG-EGFP-T2A-Luciferase transgene



6-8 week old female B6(cg)-Tyrc-2J/J mice IV-dosed with 5.0E12 VG/kg of capsid packaged with ssCAG-EGFP-T2A-Luciferase transgene

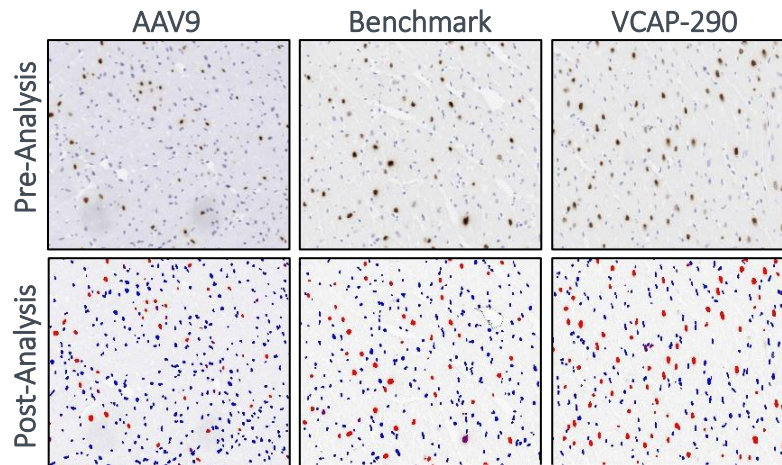
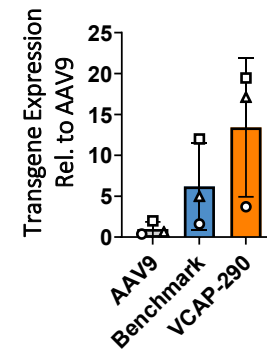
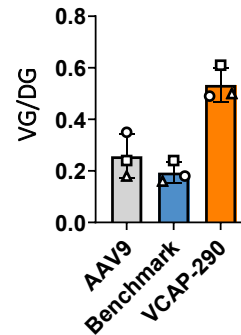
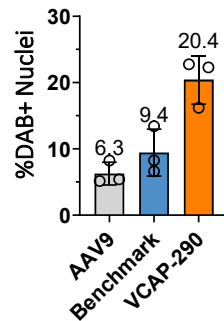
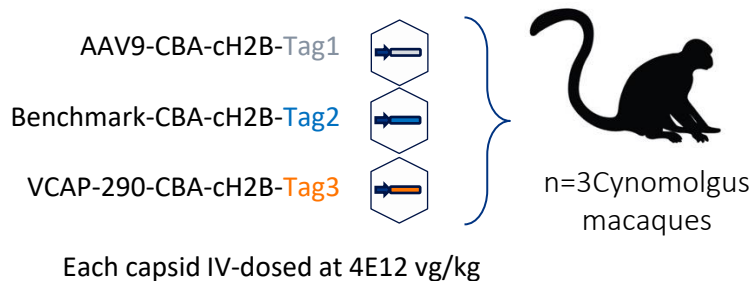
VCAP-290 Demonstrates Superior Skeletal Muscle Transduction Over AAV9 in NHPs



Pre-Analysis Image: DAB, Hematoxylin
Post-Analysis Image: Tag Protein+, Tag Protein-

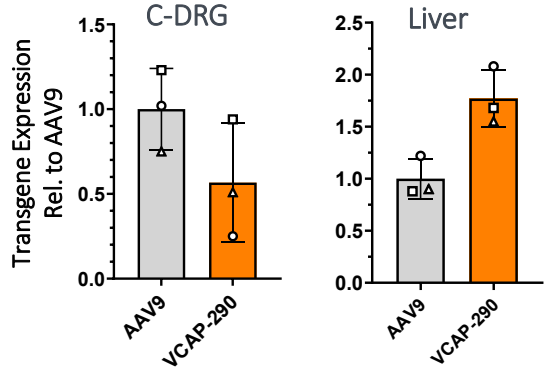
VCAP-290 Demonstrates Superior Cardiac Muscle Transduction Over AAV9 in NHPs

Heart



Pre-Analysis Image: DAB, Hematoxylin
Post-Analysis Image: Tag Protein+, Tag Protein-

Continuous Directed Evolution of VCAP-290 Allows for Selection of 2nd Generation Capsids with Improved Peripheral Tissue Detargeting

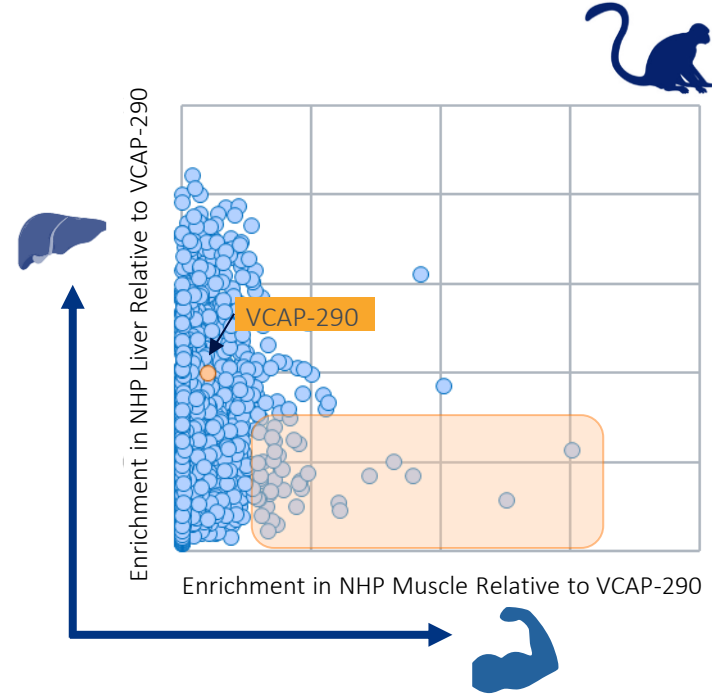
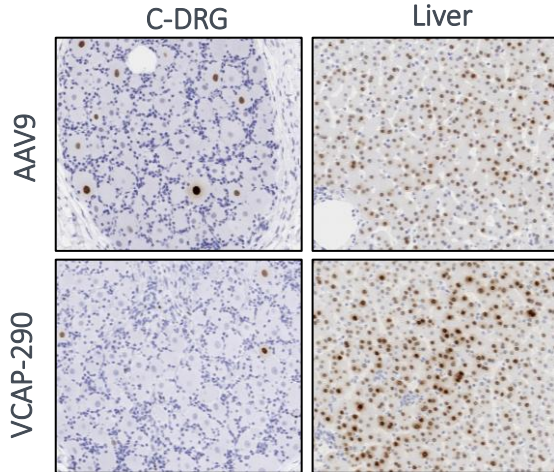


2nd Generation TRACER Evolution

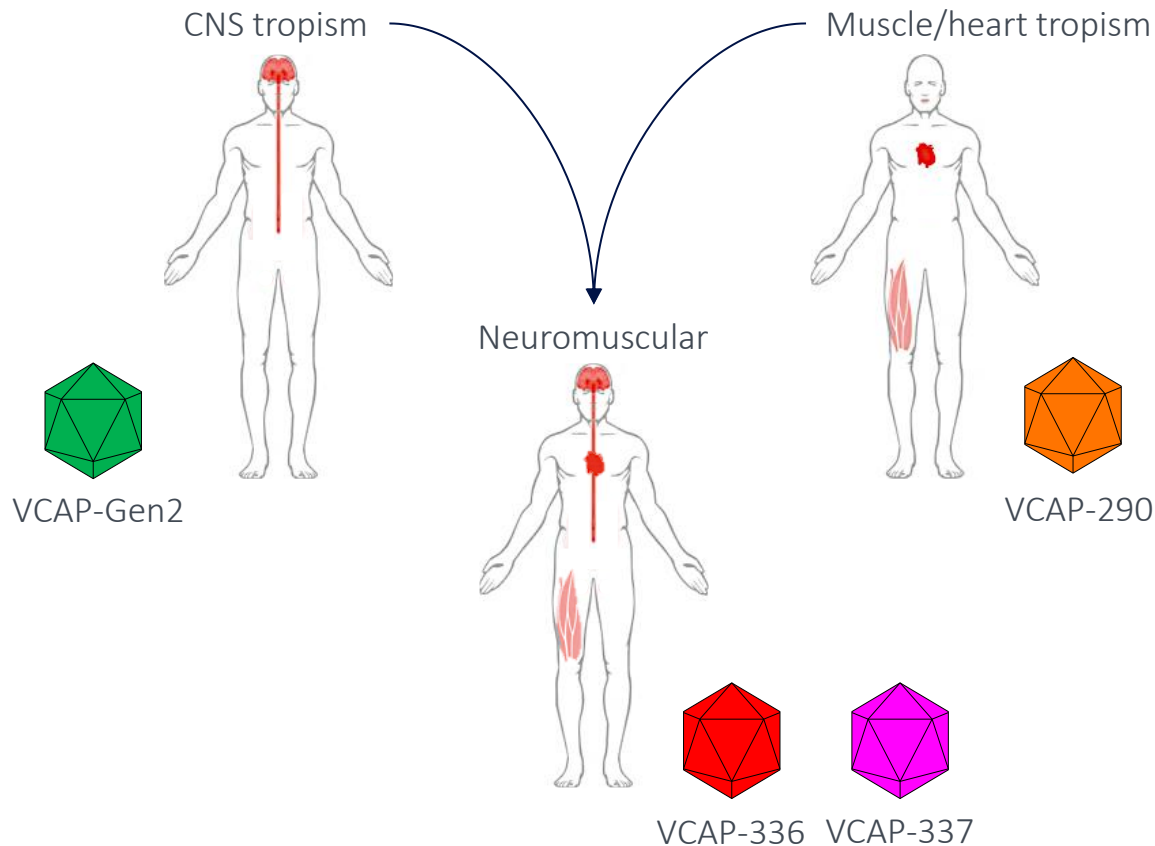


Limited Mutagenesis

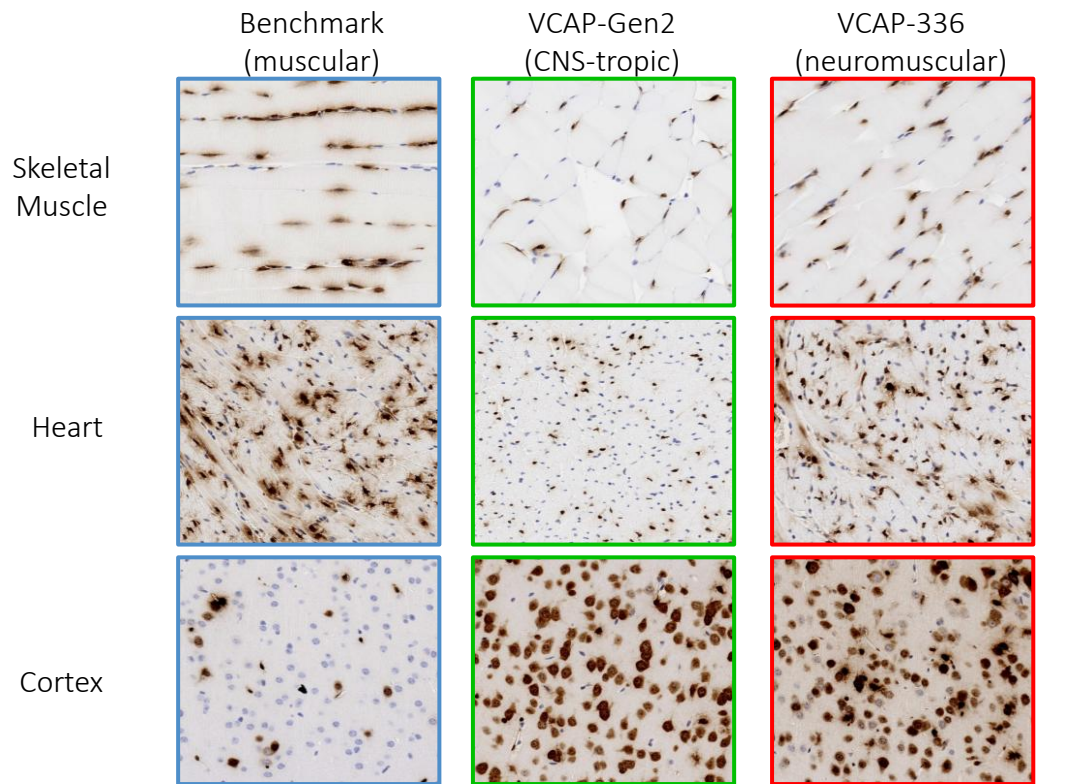
...VXAP290S**X**SEQUENCE...
 ...VCA**X**290**X**EQUENC**X**...
 ...VCAP290**X**EQUENC**X**...
 ...**X**CAP2**X**0SEQU**X**ENCE...
 ...VCAP29**X**SEQUENC**X**...
 ...V**X**AP290SEQUENCE...
 ...VCAP2**X**0SEQUENC**X**...
 ...VCA**X**290SEQU**X**X**C**...
 ...**X**C**P**290SEQUENCE...
 ...VCAP**X**90S**X**SEQUENCE...



Evolution of Multi-Tropic AAV Capsids for Neuromuscular Indications

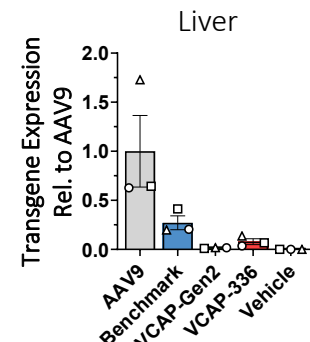
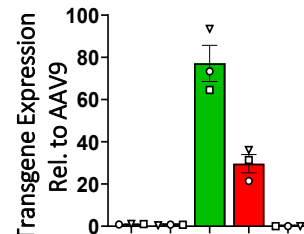
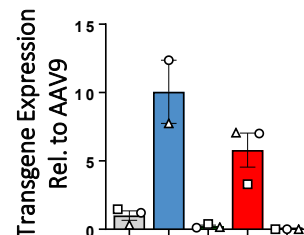
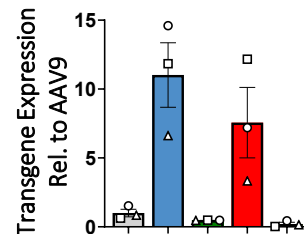


Neuromuscular Capsid VCAP-336 Demonstrates Dual Tropism to Muscle and the CNS in Mice

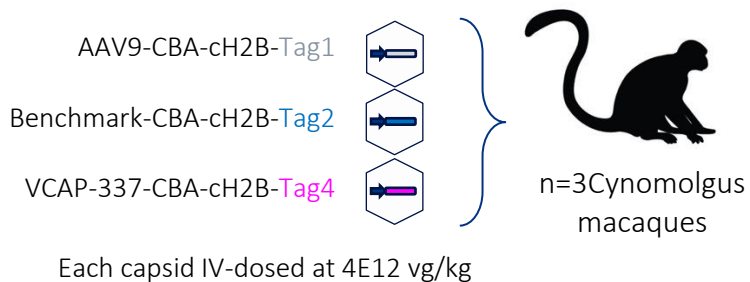


6-8 week old female Balb/c mice IV-dosed with 1E13 VG/kg of capsid packaged with scCAG-H2B-HA-transgene

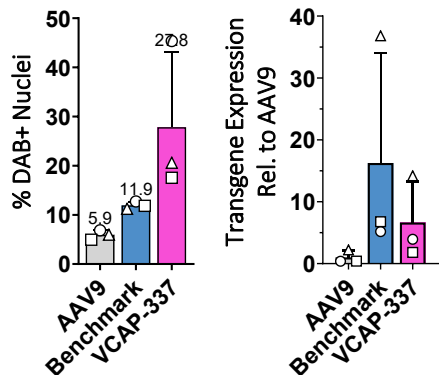
Anti-HA IHC



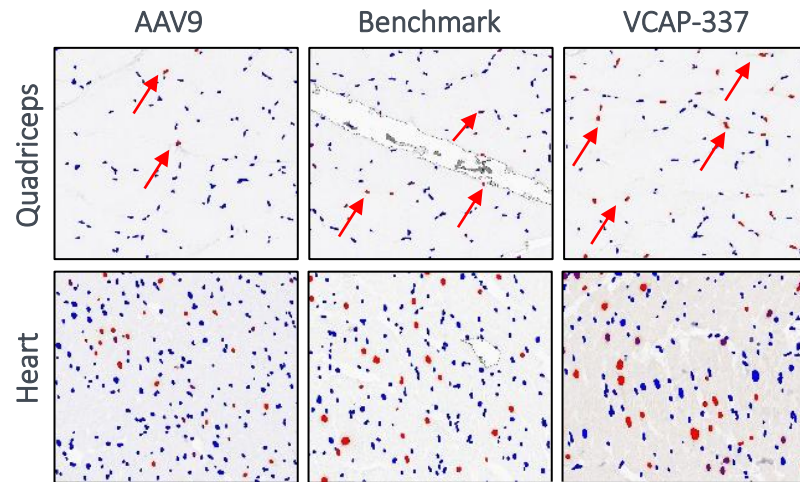
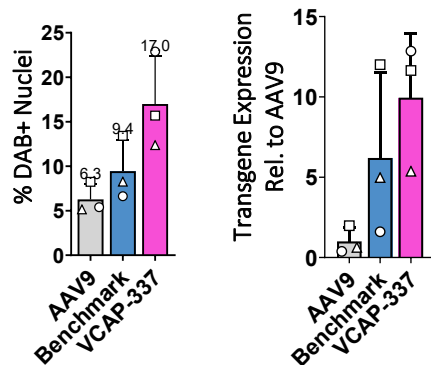
Neuromuscular Capsid VCAP-337 Retains Tropism to Muscle in NHPs



Quadriceps



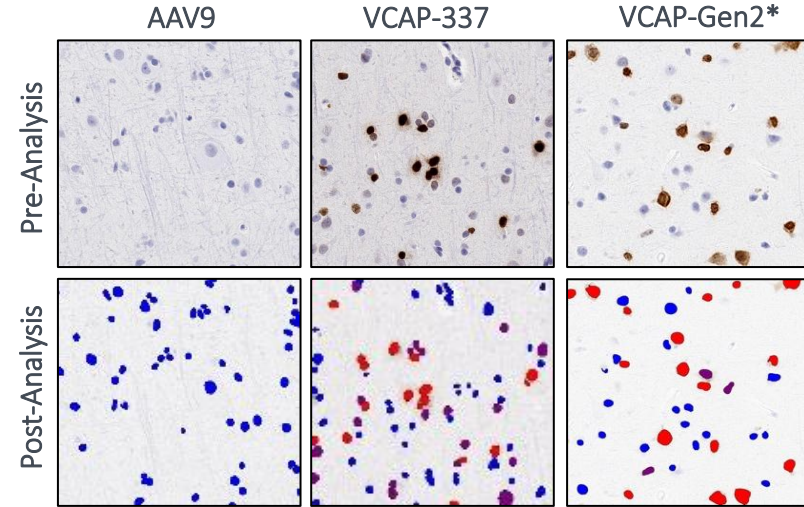
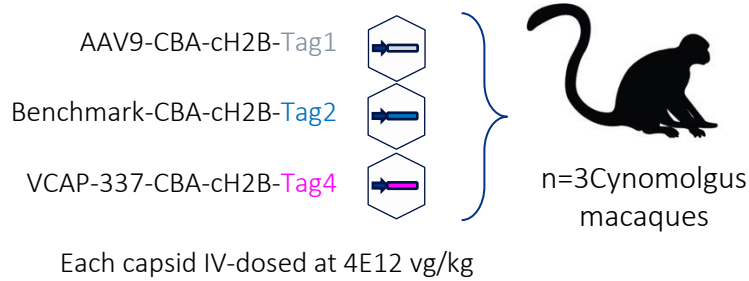
Heart



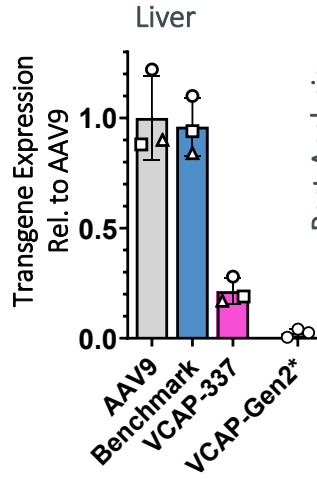
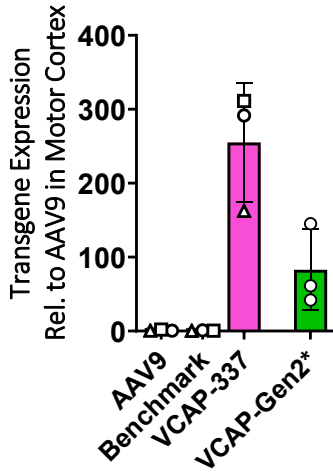
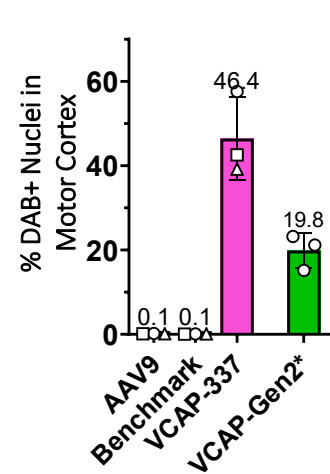
Post-Analysis Image: Tag Protein+, Tag Protein-

Neuromuscular Capsid VCAP-337 Demonstrates Higher CNS Tropism than VCAP-Gen2

Motor Cortex



Post-Analysis Image: Tag Protein+, Tag Protein-
Representative Images from layer V of motor cortex



- VCAP-290 demonstrates strong tropism to skeletal and cardiac muscles in both mice and non-human primates compared to AAV9.
 - ~100X over AAV9 in mouse skeletal muscle
 - ~10X over AAV9 in mouse cardiac muscle
 - ~25X over AAV9 in NHP skeletal muscle
 - ~13X over AAV9 in NHP cardiac muscle
- VCAP-290 targets 100% of muscle fibers in mice at a low dose of 5E12.
- Neuromuscular capsids VCAP-336 and VCAP-337 effectively transduce both muscle and CNS
- Neuromuscular capsids demonstrate strong liver detargeting properties similar to Voyager's best CNS-tropic capsids.

Acknowledgements



Capsid Discovery

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Amy Bruce
Rong Zhao

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Jordan Routhier
Tim Fiore
Ruohong Zhou
Dhiral Shah

Bioanalytics

Jeff Thompson
Joseph Clement
Rebecca Spellman

Data Science

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Jeron Chen

Neuroscience

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Cassie Retzlaff
Meg Dalrymple
Maneesha Paranjpe
Charlotte Chung

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Su Jing Chan
Johnny Yao
Alex Kutchin

Legal/IP

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Questions?

