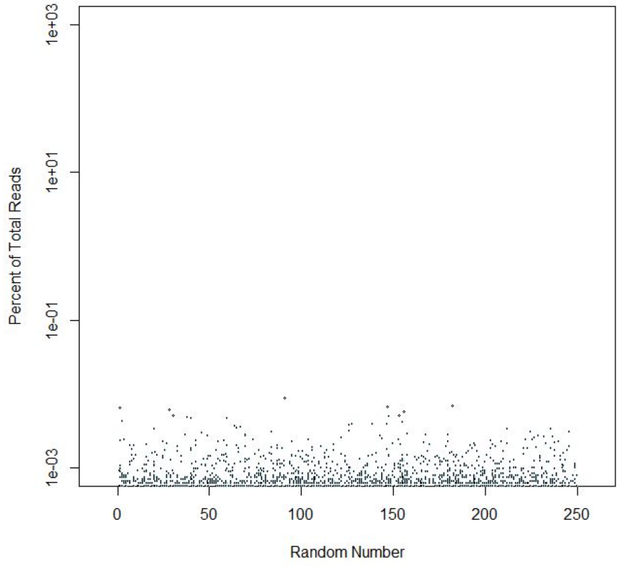
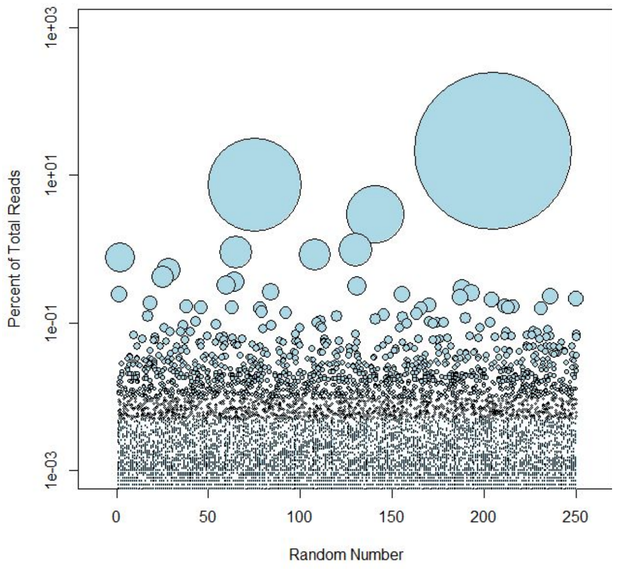
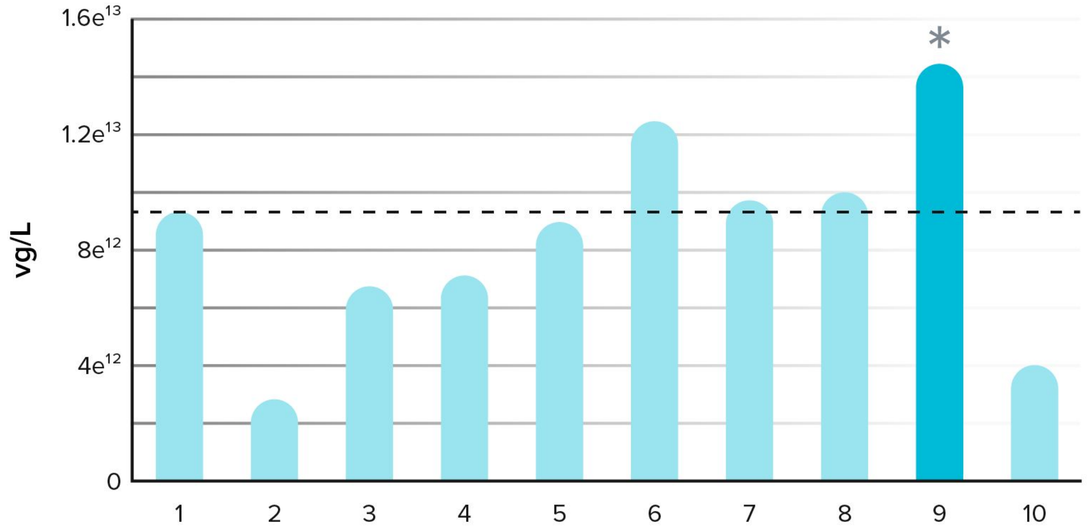
# STRV16: Multiple loop modifications to obtain a muscle-specific capsid

## Round 1 Input




## Round 3 Output




Developed as **part of muscle program**

Capsid Library **evolved over 3 rounds** in NHPs via IV administration and AAV genome isolation from muscle tissue

VR-VIII and VR-IV substitutions made both simultaneously and sequentially in different rounds

STRV16 selected for manufacturability and **best muscle transduction profile** in mice among selected leads

# STRV16: Animal studies summary

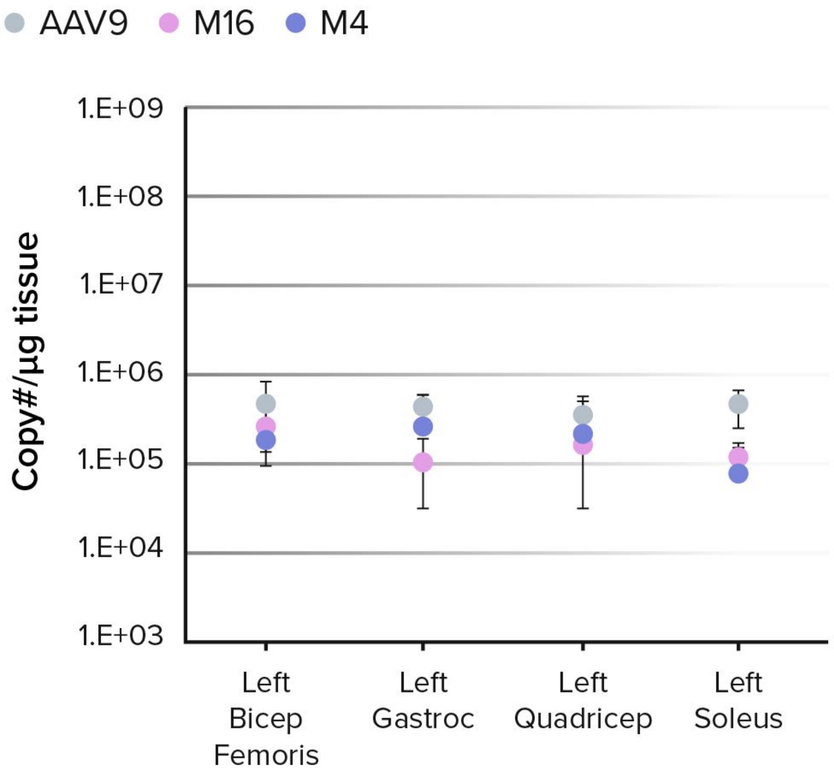
| Capsid | Animal | RoA | Dose | Key Findings |
|---|---|---|---|---|
| **STRV16** | NHP | IV+ICM | 4.5e13 vg/kg | **Comparable skeletal muscle transduction** to wt9<br><br>**≥10x lower transduction of off-target tissues**, **1000x lower liver targeting** than wt9 |
| | Mouse | IV | 1e13 vg/kg | **Liver de-targeting compared to wt9**<br><br>**No improvement over wt9 in muscle tissue transduction** (*primarily because of the NHP-only evolution strategy*) |

VCN: Vector Copy Number

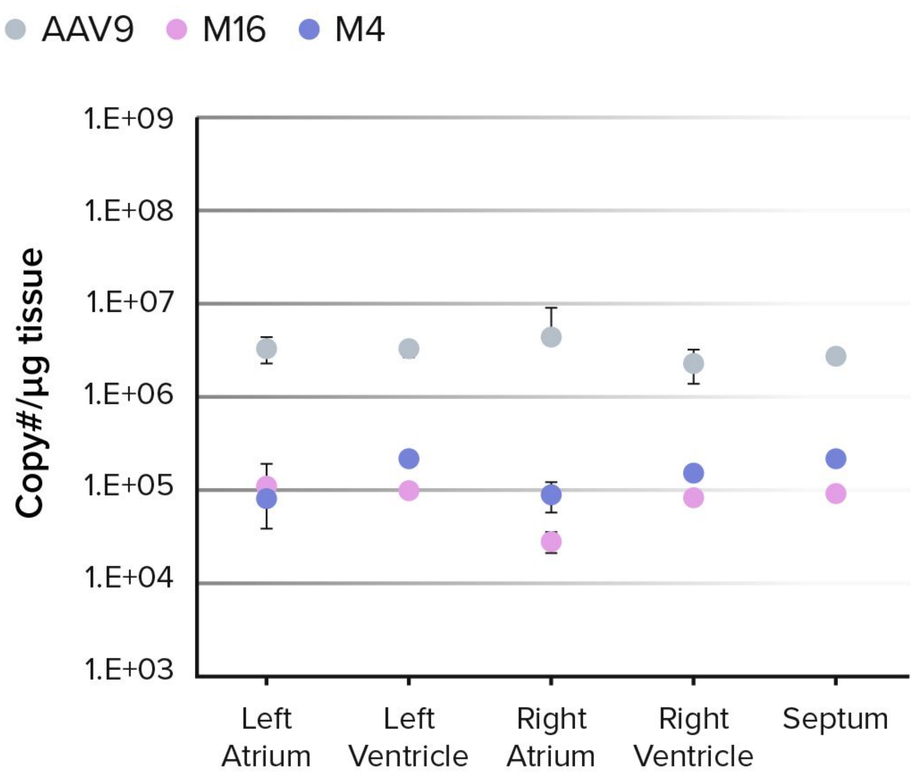
# STRV16 and STRV4 maintain muscle tropism with reduced localization to heart

STRV16 and STRV4 advanced to NHPs via dual route of administration (5e13 vg/kg IV; ~1e13vg ICM)

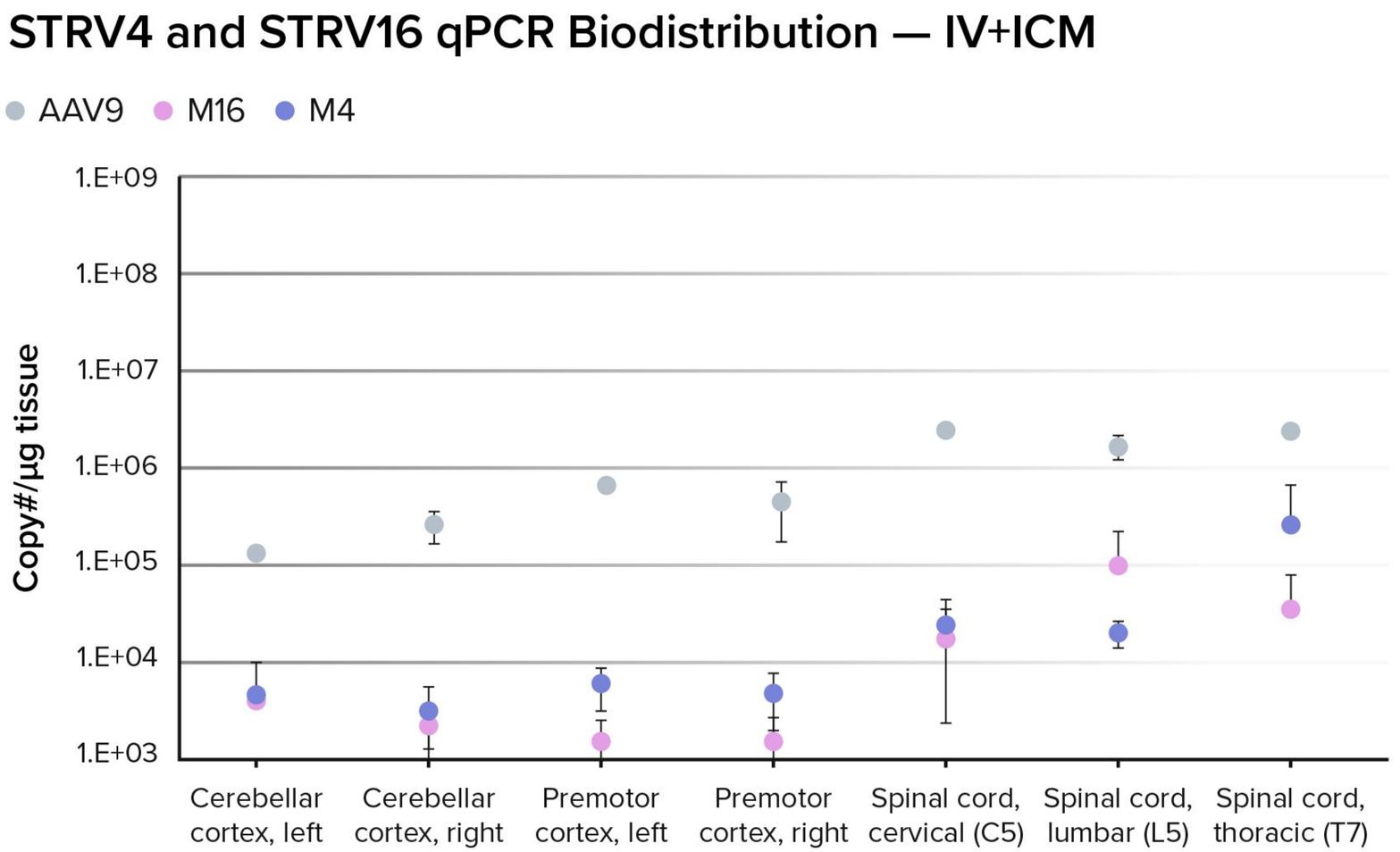
## STRV4 and STRV16 qPCR Biodistribution – IV+ICM Muscle



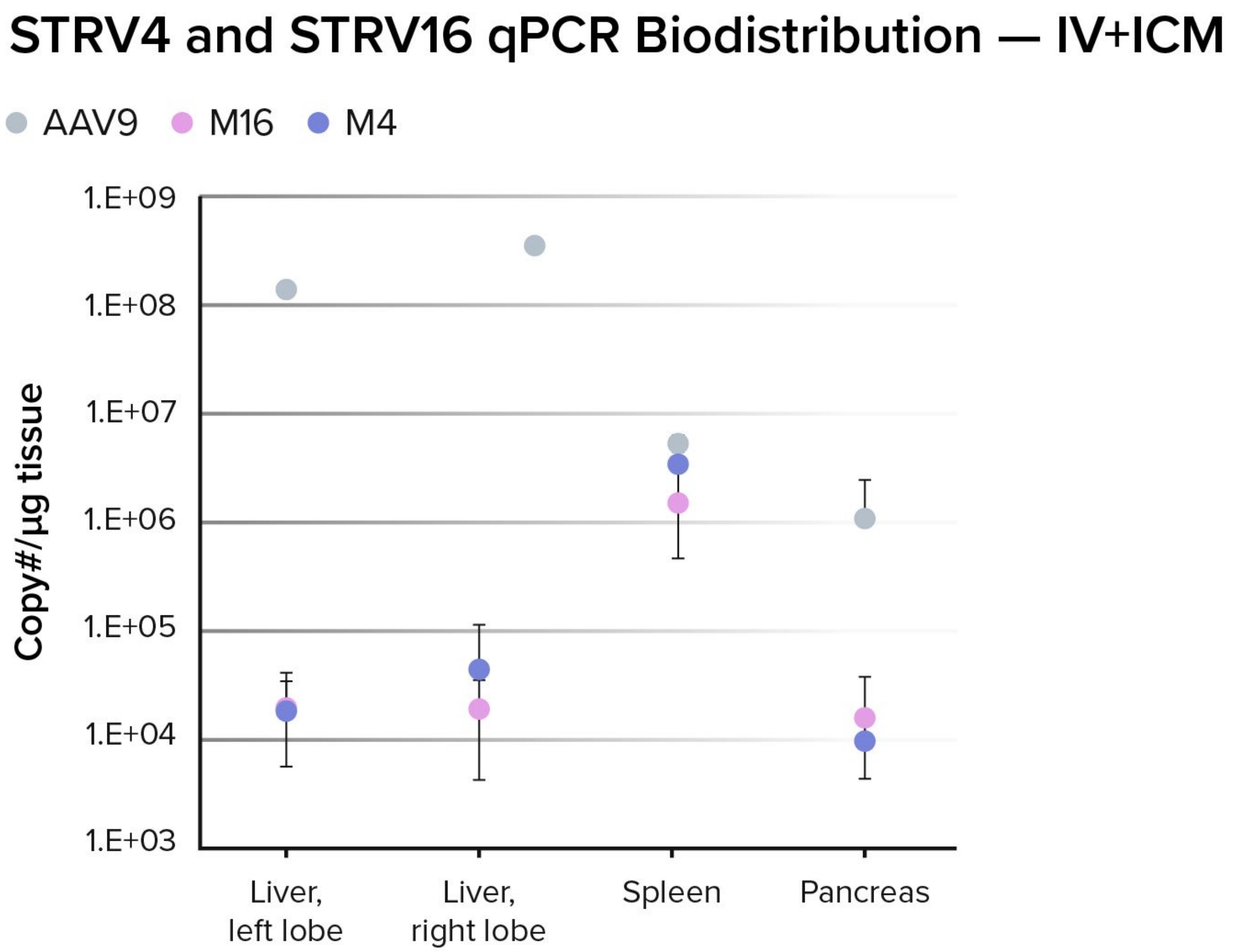

## STRV4 and STRV16 qPCR Biodistribution – IV+ICM Heart



# Similar reduction in localization to CNS



# And >1000X lower liver tropism as compared to AAV9



# To improve potency or expand tropism combine peptide insertion on an evolved capsid with a cross-species approach

- STRV16i developed as part of continued **evolution of STRV muscle capsids**
- Capsid Library **re-evolved over 2 rounds in NHPs and mice via IV administration and AAV genome isolation from muscle or heart tissue**
  - Two cross-species approaches used, resulting in 3 libraries in total
- 35+ select sequences isolated and cloned for *in vivo* testing
  - **Only one of those select sequences contain an RGD motif**, circumventing potential future IP issues
  - 10,000+ sequences ready for discovery and development