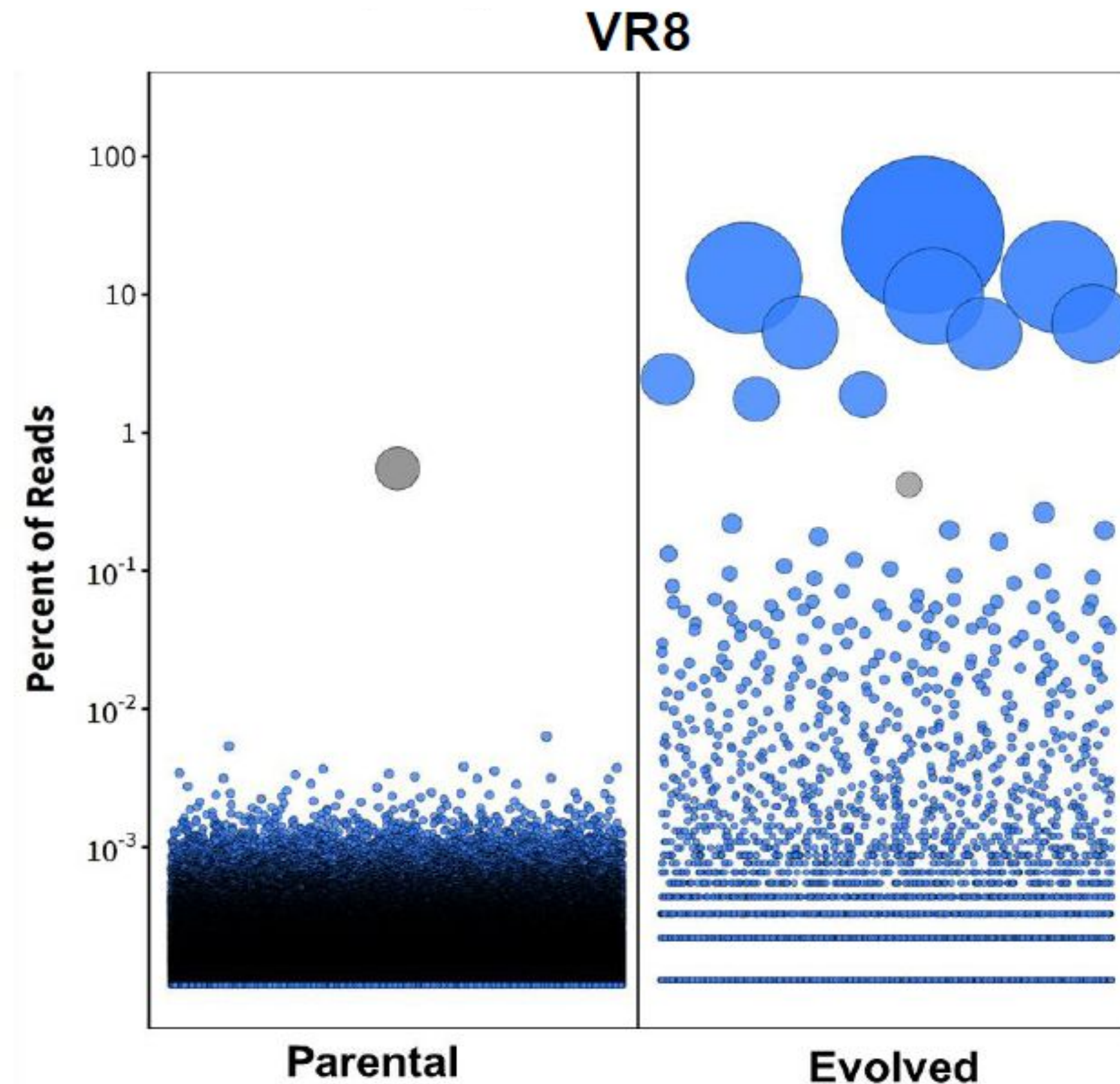


STRV84 capsid evolution



STRV84 developed in conjunction with the Asokan Lab @ Duke University through **cross-species evolution of AAV9**

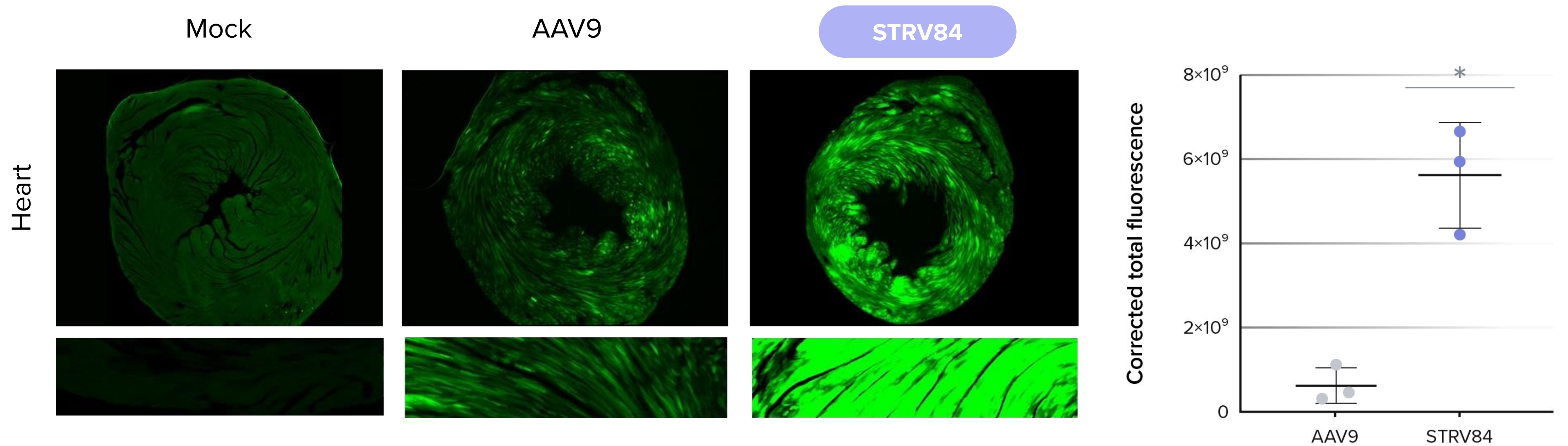
Capsid Library **evolved across multiple species – Mouse and Pig**

STRV84 selected from top **enriched sequences in brain and spinal cord** and advanced for animal testing

STRV84: Animal studies

Animal	RoA	Dose	Cargo & Readout	Key Findings
Mouse (C57BL/6)	IV	5e13 vg/kg	scCbh-eGFP IHC and image quantitation	Improved neuronal transduction compared to wt9; reduced astrocyte transduction Improved transduction in the heart compared to wt9
Mouse	ICV	2e10 vg	scCbh-eGFP Fluorescence and co-localization	Improved transduction compared to wt9
Pig	IT	3e13 vg	scCbh-eGFP IHC	Improved neuronal transduction, especially in cortex
Pig	IC	1e14 vg		Cardiomyocyte transduction across entire heart
NHP (Cyno)	ICM	1e13 vg	mCherry IHC, qPCR	Liver de-targeting; little to no immune cell infiltration

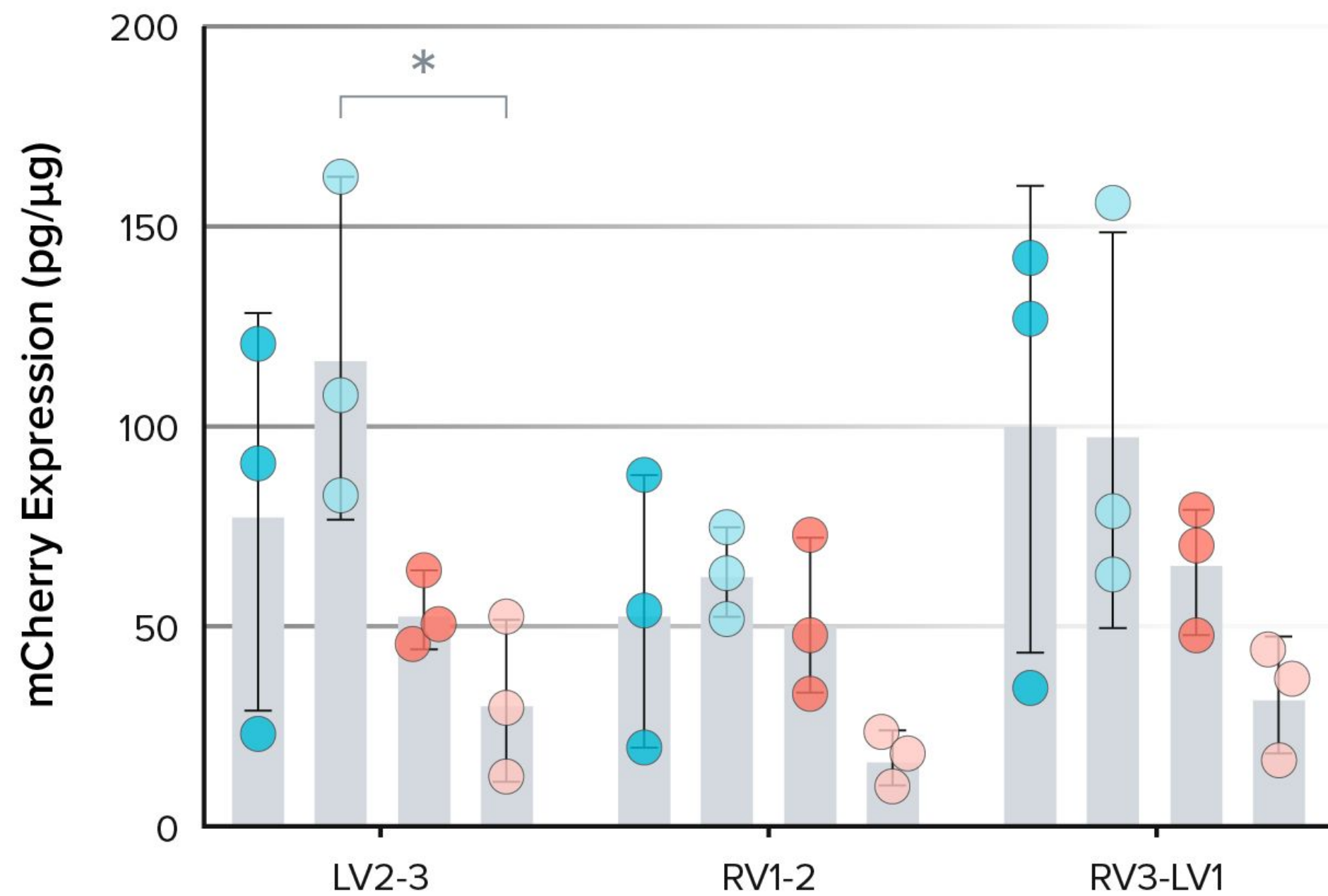
STRV84 demonstrates enhanced cardiac tropism in mice vs. AAV9



STRV84 demonstrates robust cardiac tropism in pigs

Heart Ring 2 ELISA

- Fast antegrade ● Slow antegrade
- Fast retrograde ● Slow retrograde



Heart Ring 2 VCN

- Fast antegrade ● Slow antegrade
- Fast retrograde ● Slow retrograde

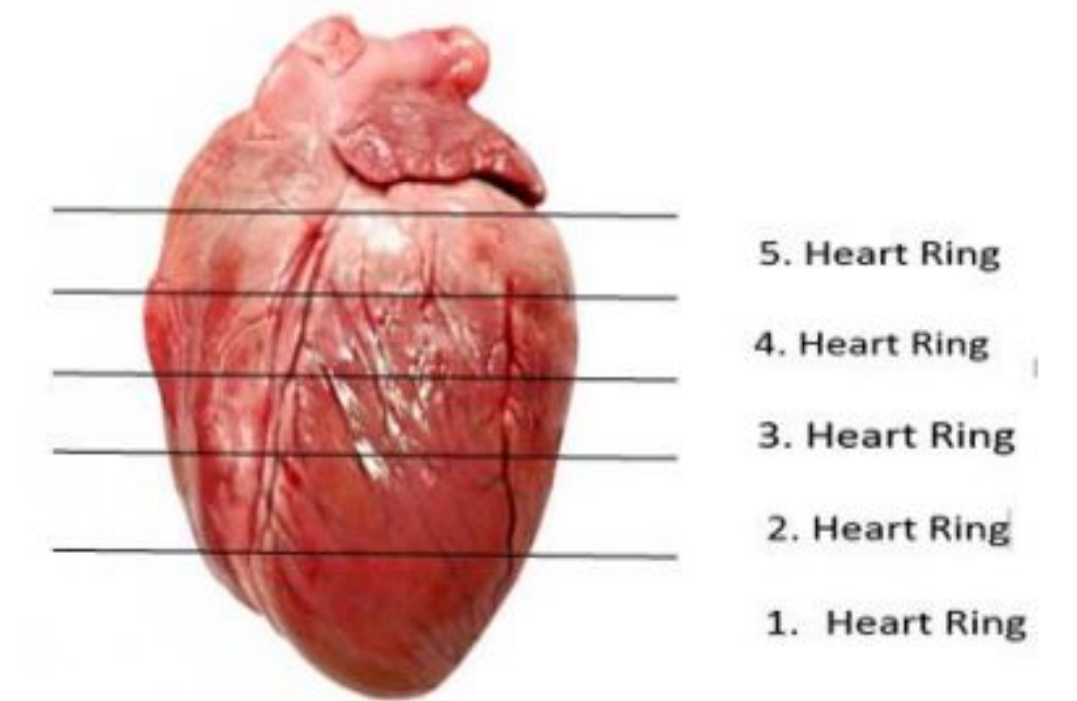
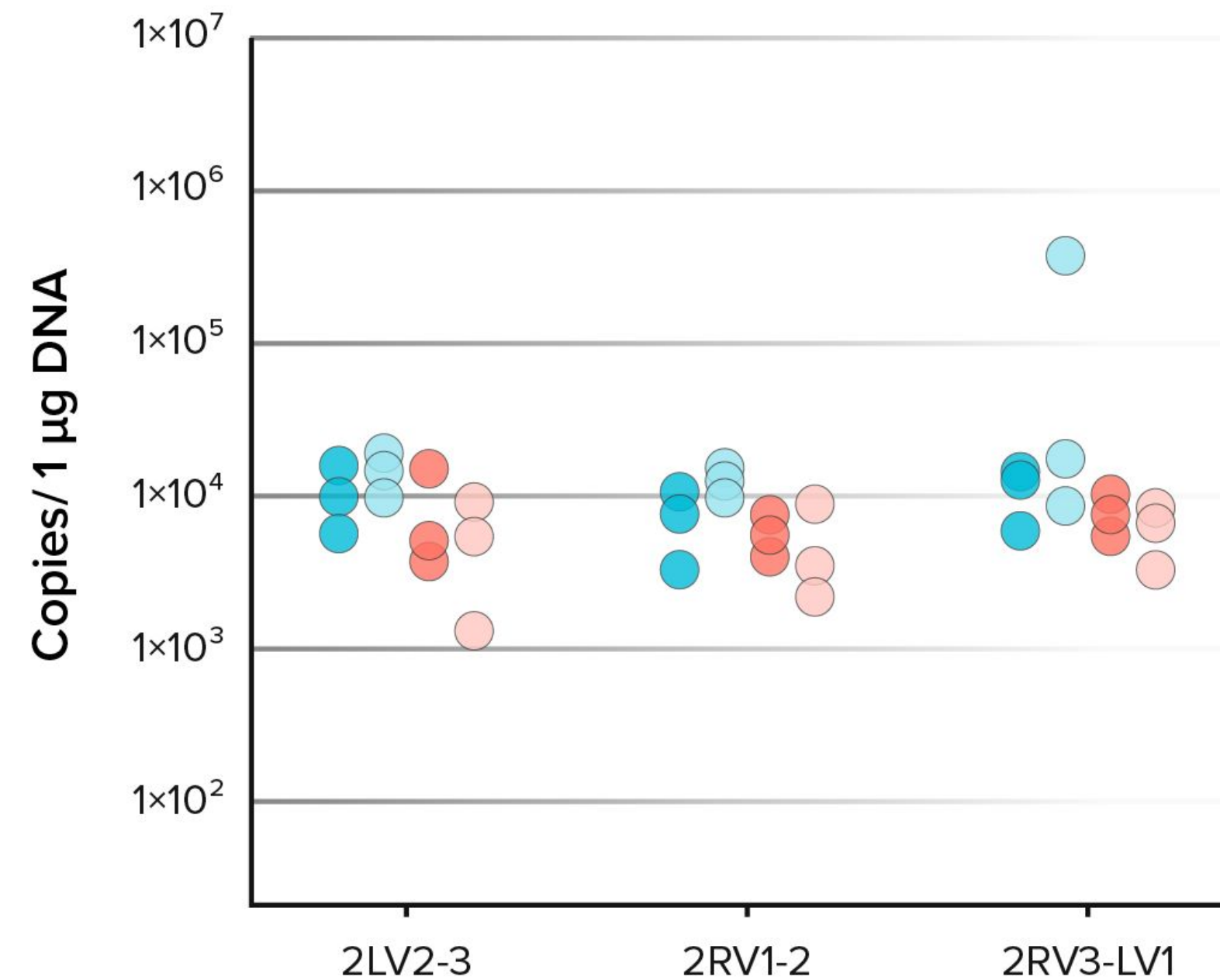
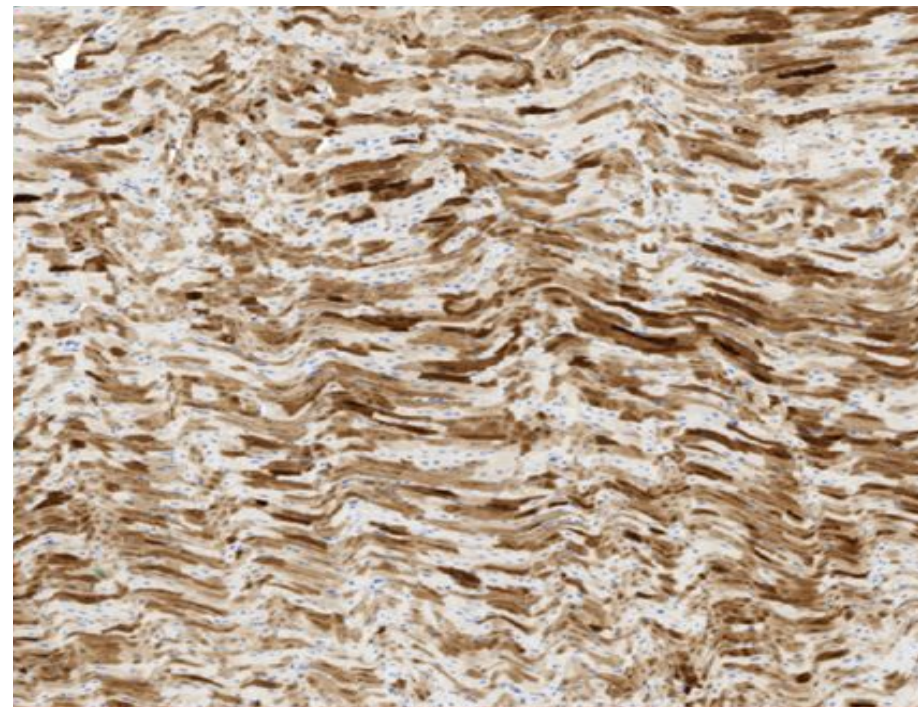


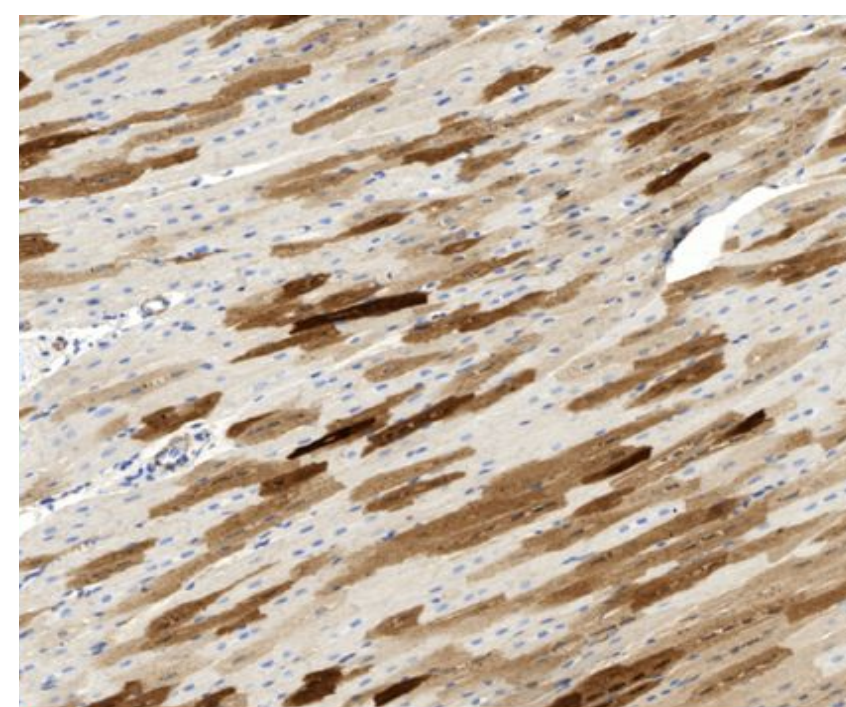
Figure 2. Heart Sectioning Schematic

STRV84 demonstrates robust cardiac tropism in pigs

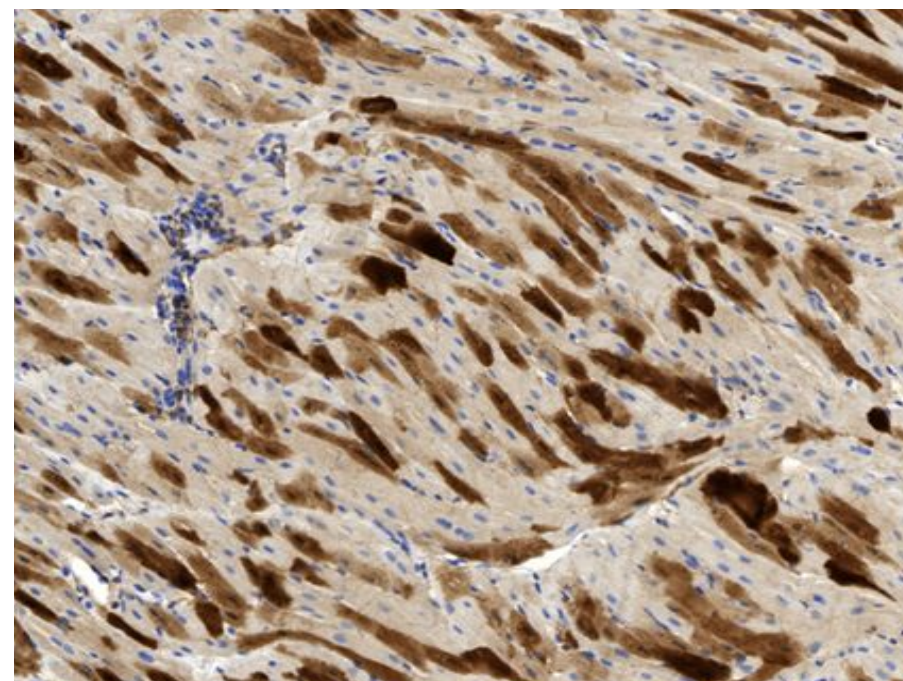
LV1-2 - Ring 2



R1-2 - Ring 2



RV3-LV1 – Ring 2



Vehicle

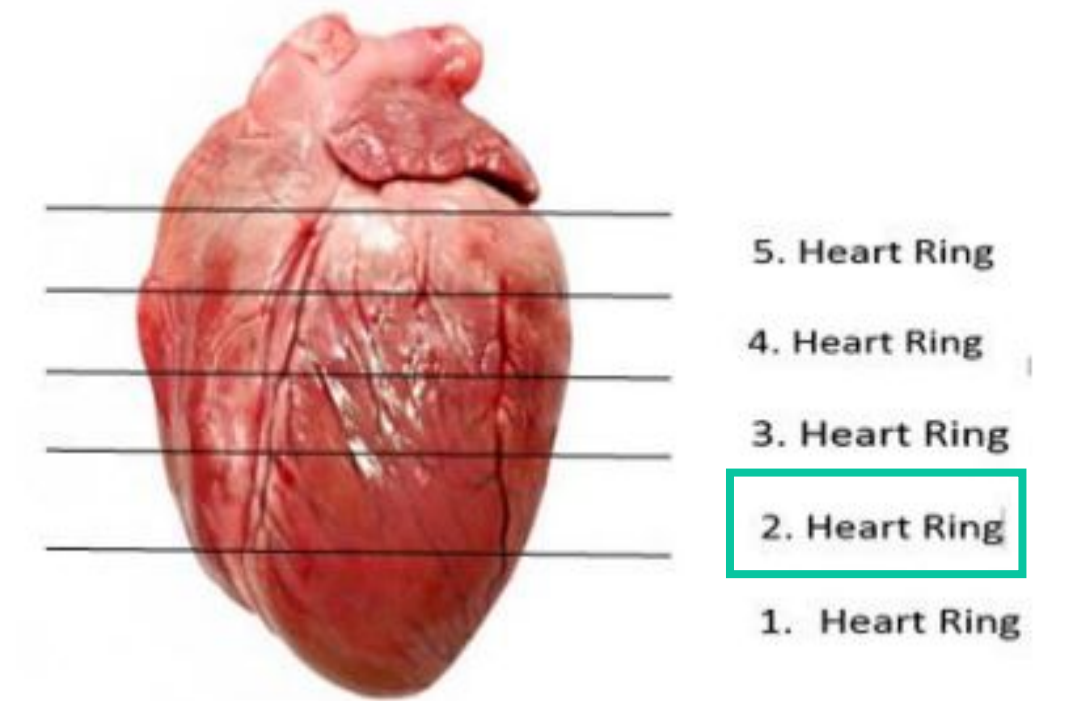
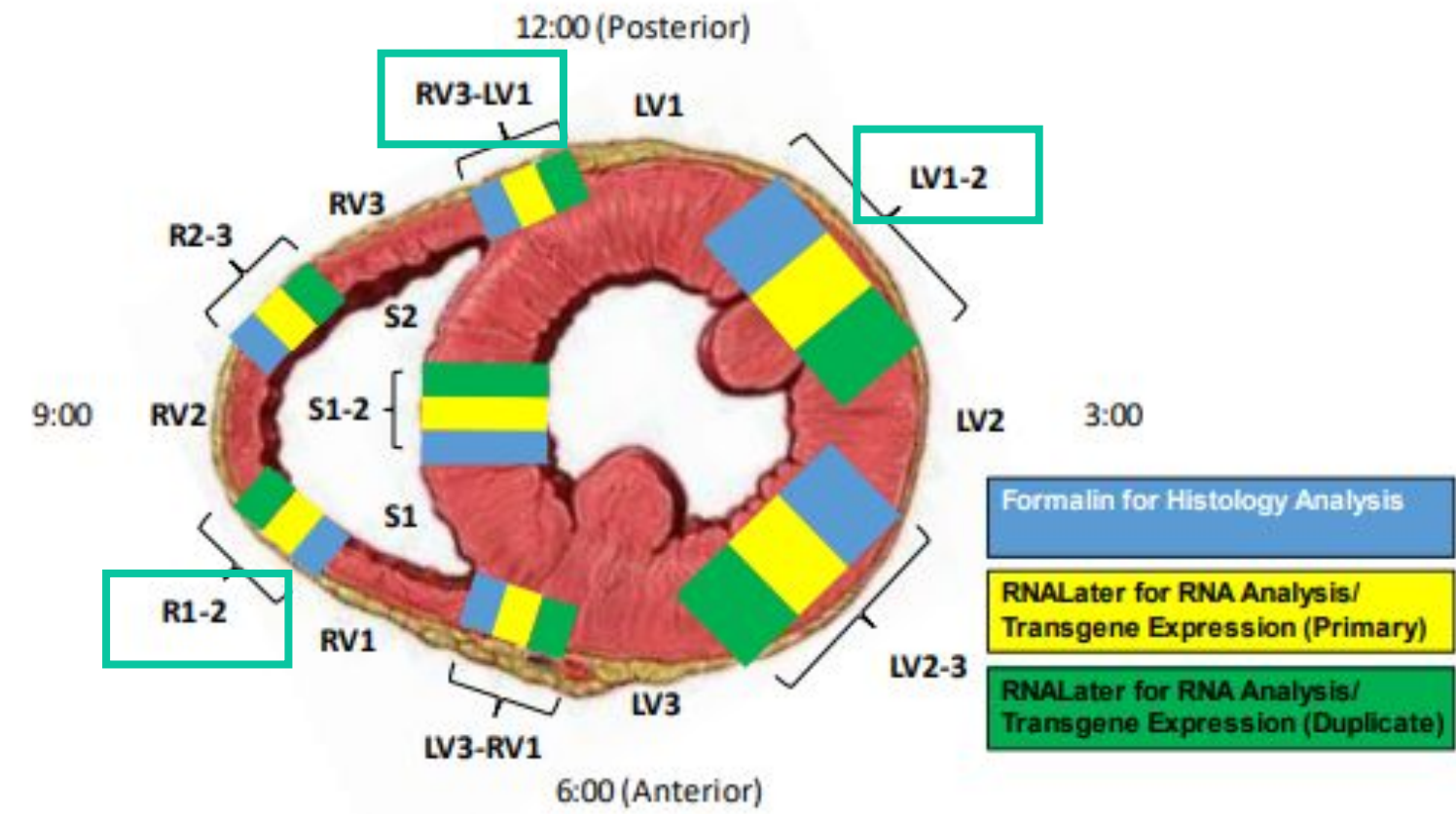
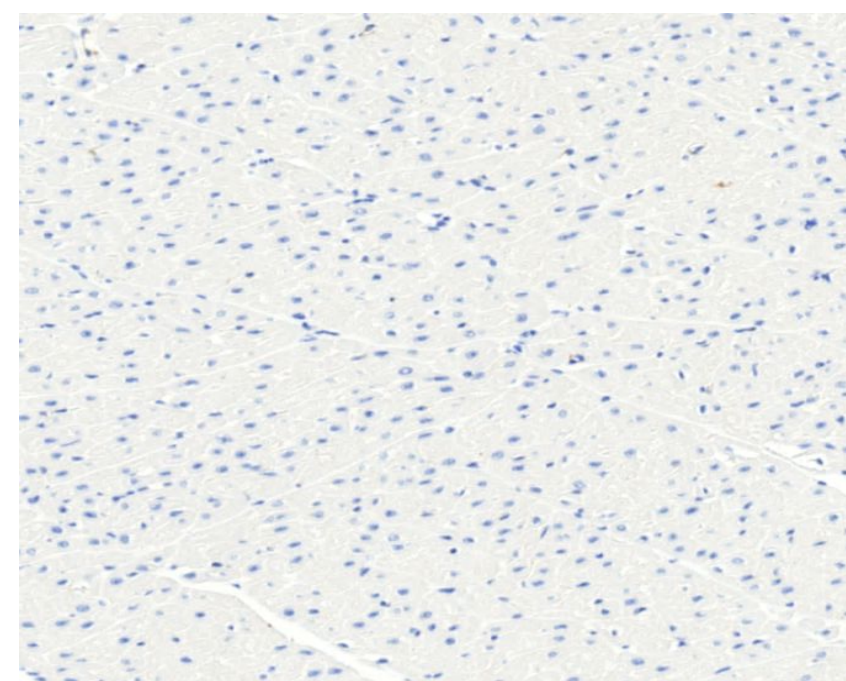
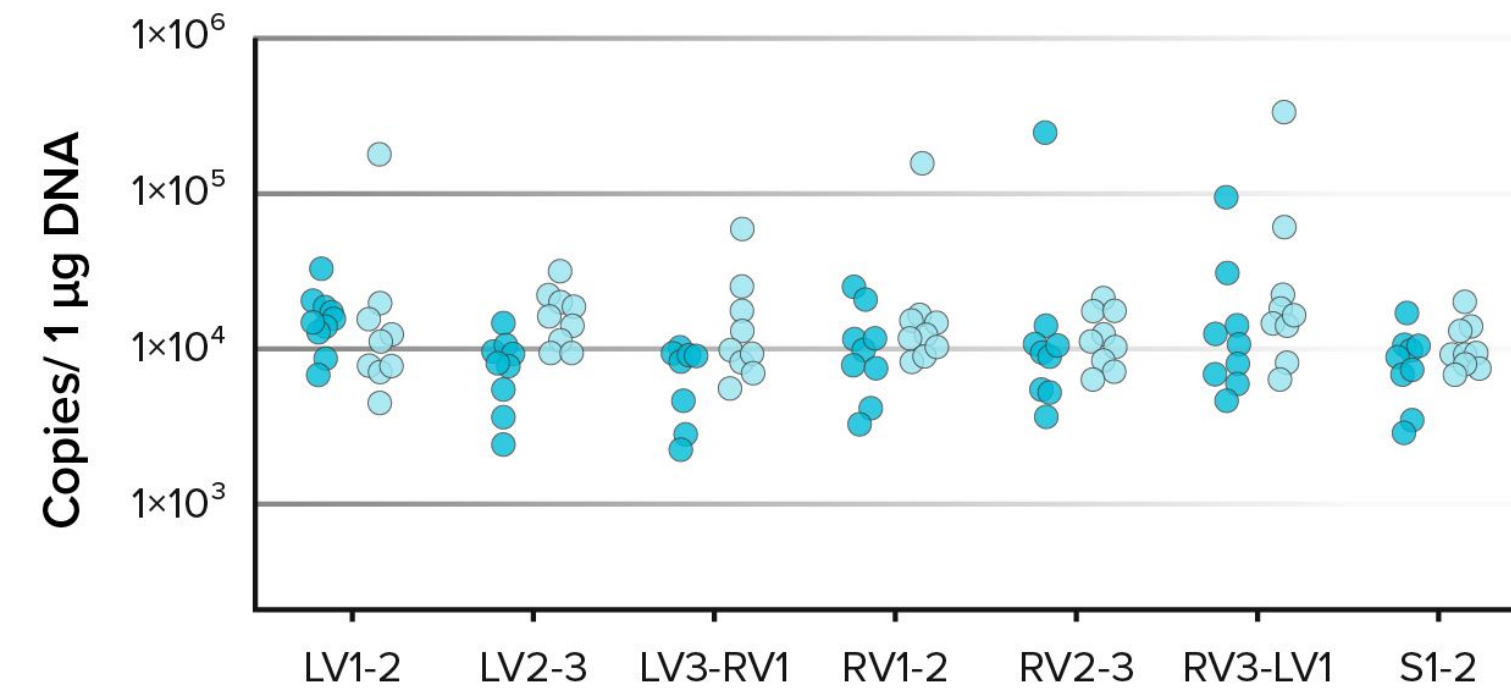


Figure 2. Heart Sectioning Schematic

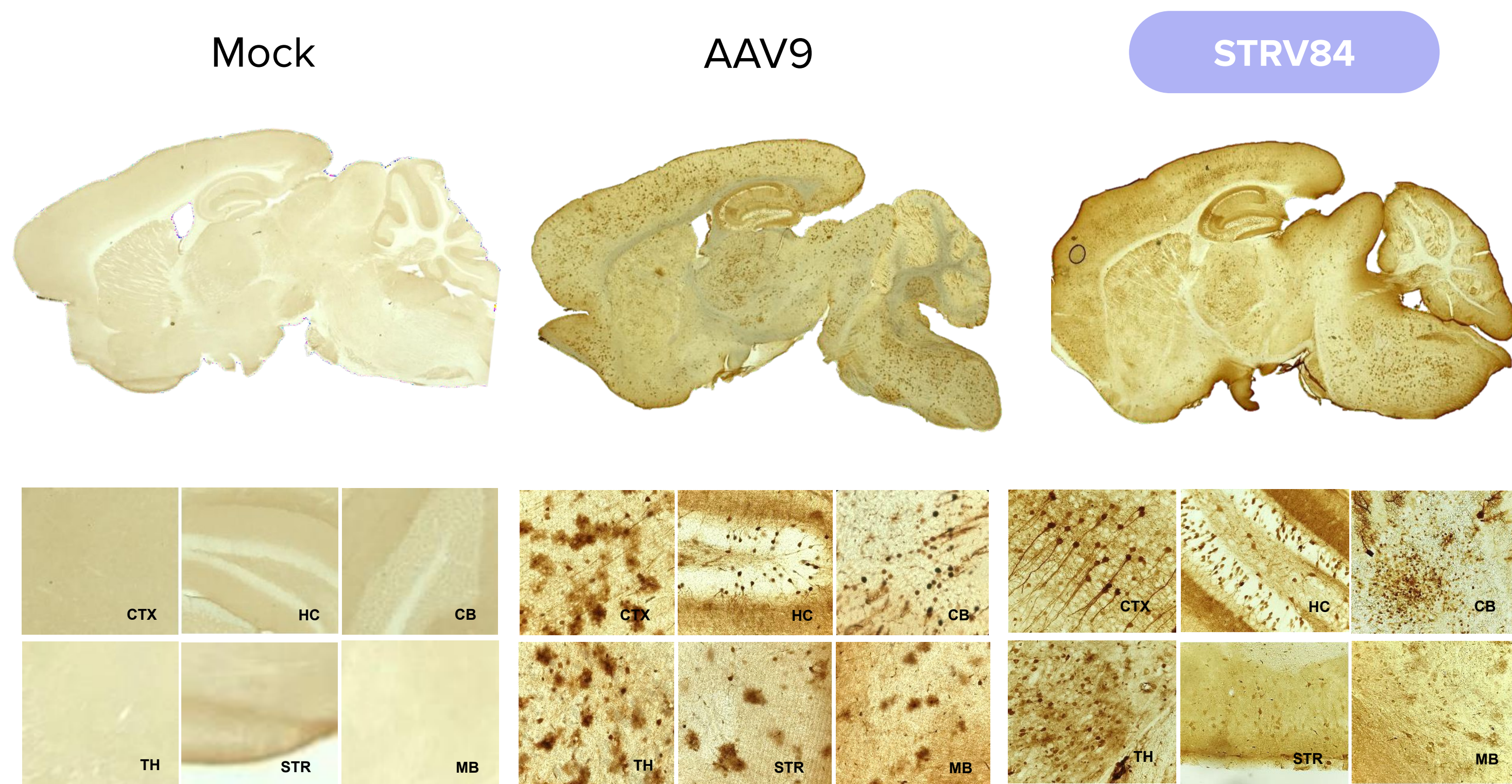
Rings Combined VCN

● Fast antegrade ● Slow antegrade



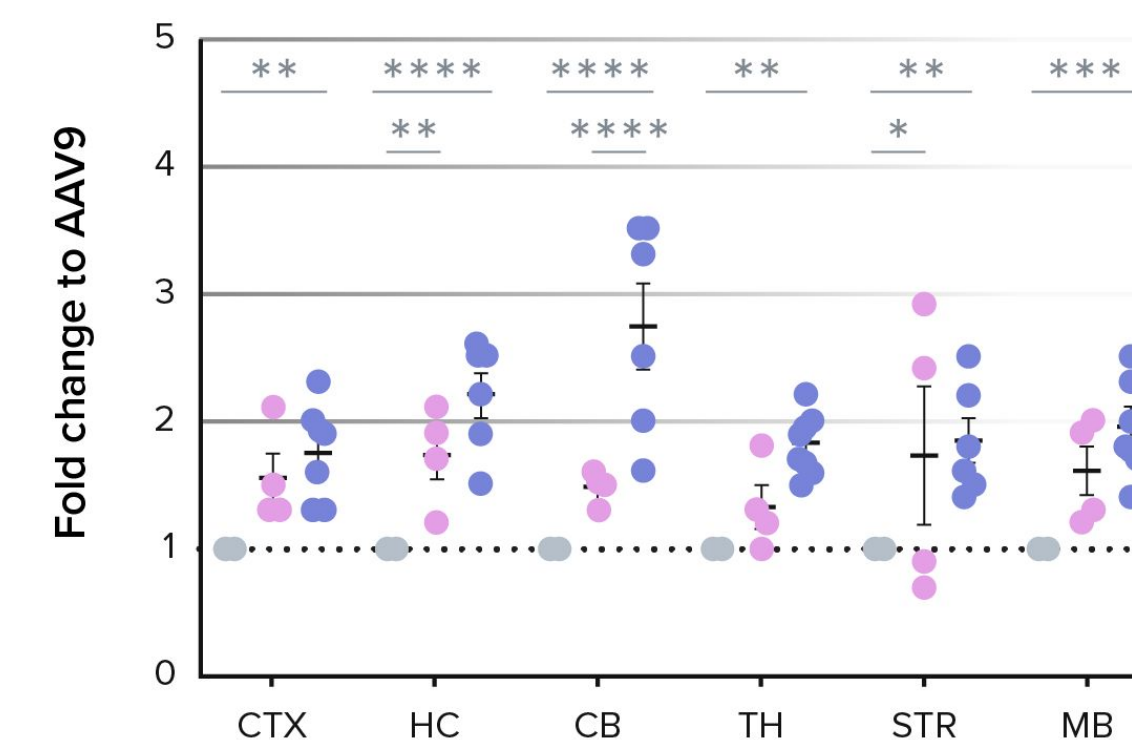
Enhanced cell-type specificity of STRV84 vs. AAV9 in mice

STRV84 exhibits increased neuronal cell-type specificity in mouse brain compared to AAV9 after IV administration



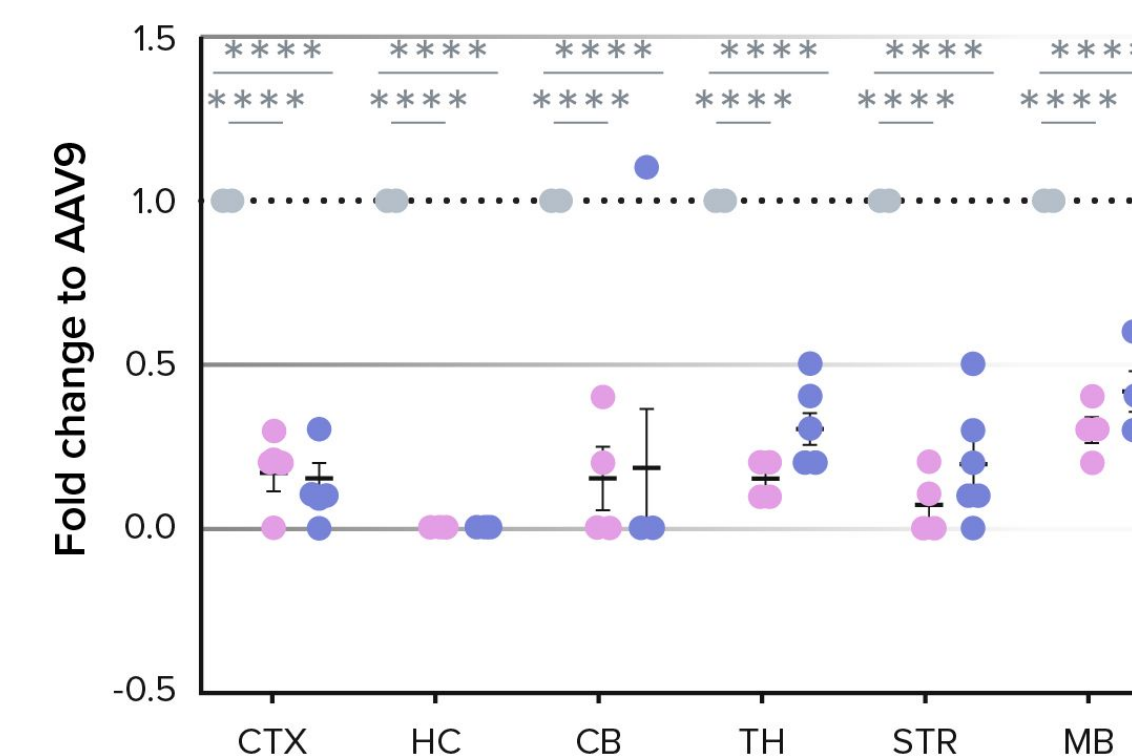
Neurons

● AAV9 ● STRV81 ● STRV84



Astrocytes

● AAV9 ● STRV81 ● STRV84



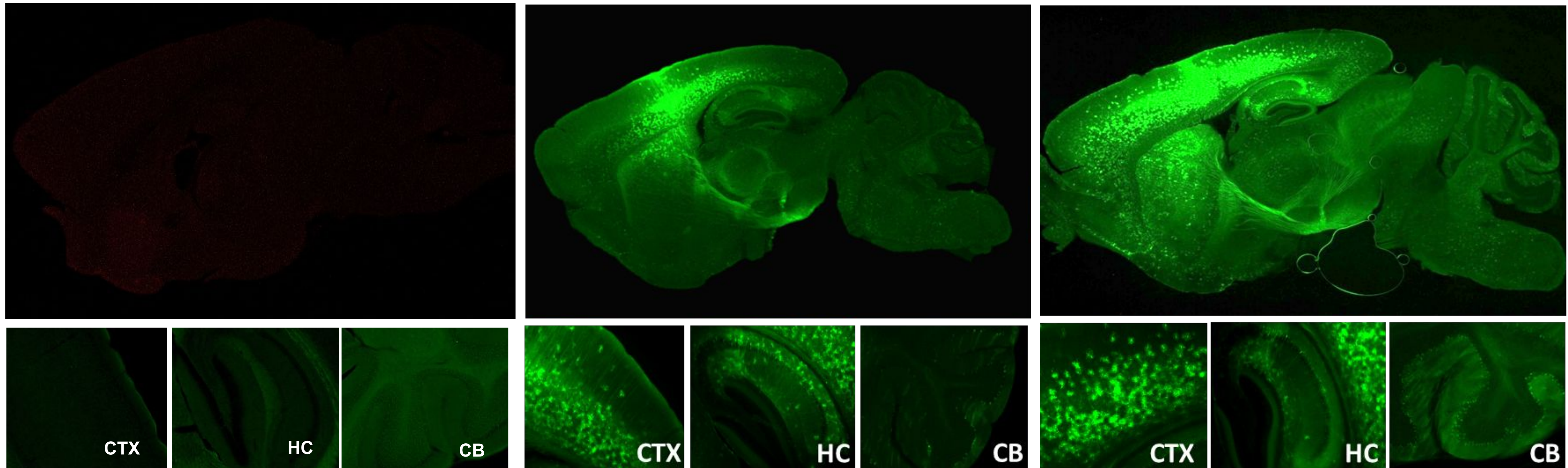
Enhanced cell-type specificity of STRV84 vs. AAV9 in mice

STRV84 exhibits increased neuronal cell-type specificity in mouse brain compared to AAV9 after IV administration

Mock

AAV9

STRV84

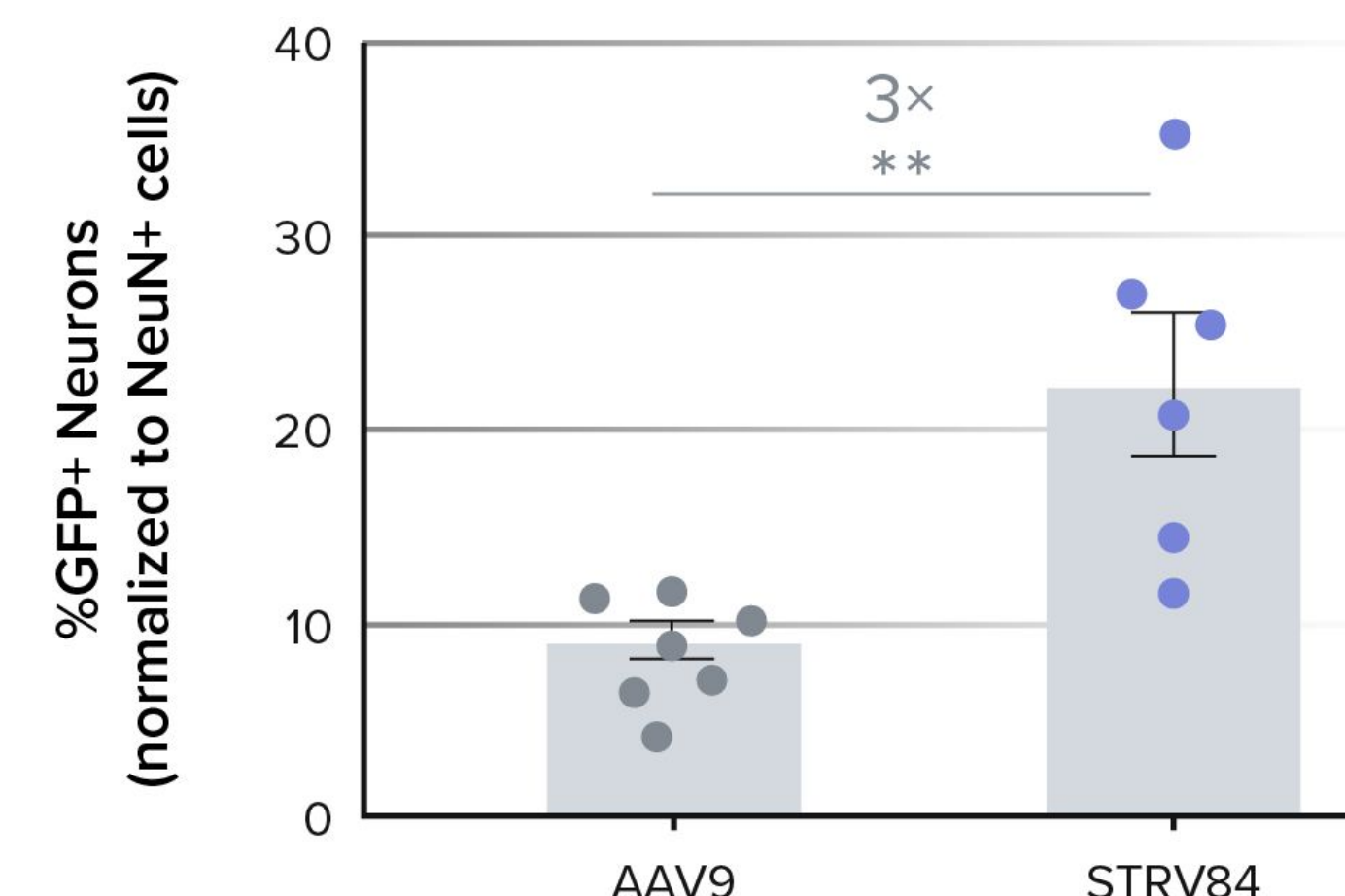
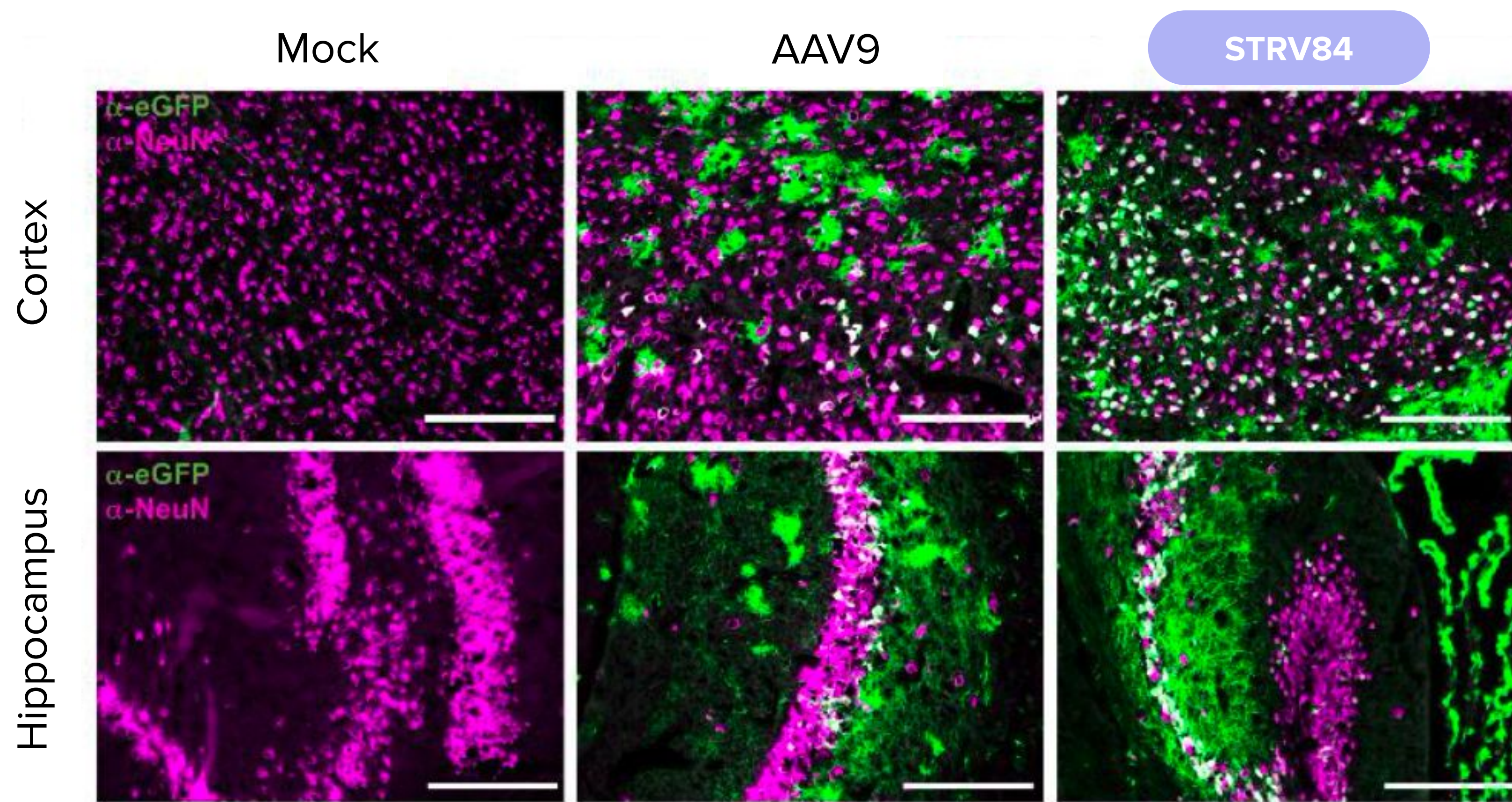


Organism: Mouse | ROA: IV injection | Dose: 5×10^{13} vg/kg | Duration: 4 weeks

ROA: route of administration; ICV: intracerebroventricular; CTX: cortex;
HC: hippocampus; CB: cerebellum; vg: viral genomes.

Enhanced cell-type specificity of STRV84 vs. AAV9 in mice

STRV84 exhibits increased neuronal cell-type specificity in mouse brain compared to AAV9 after IV administration

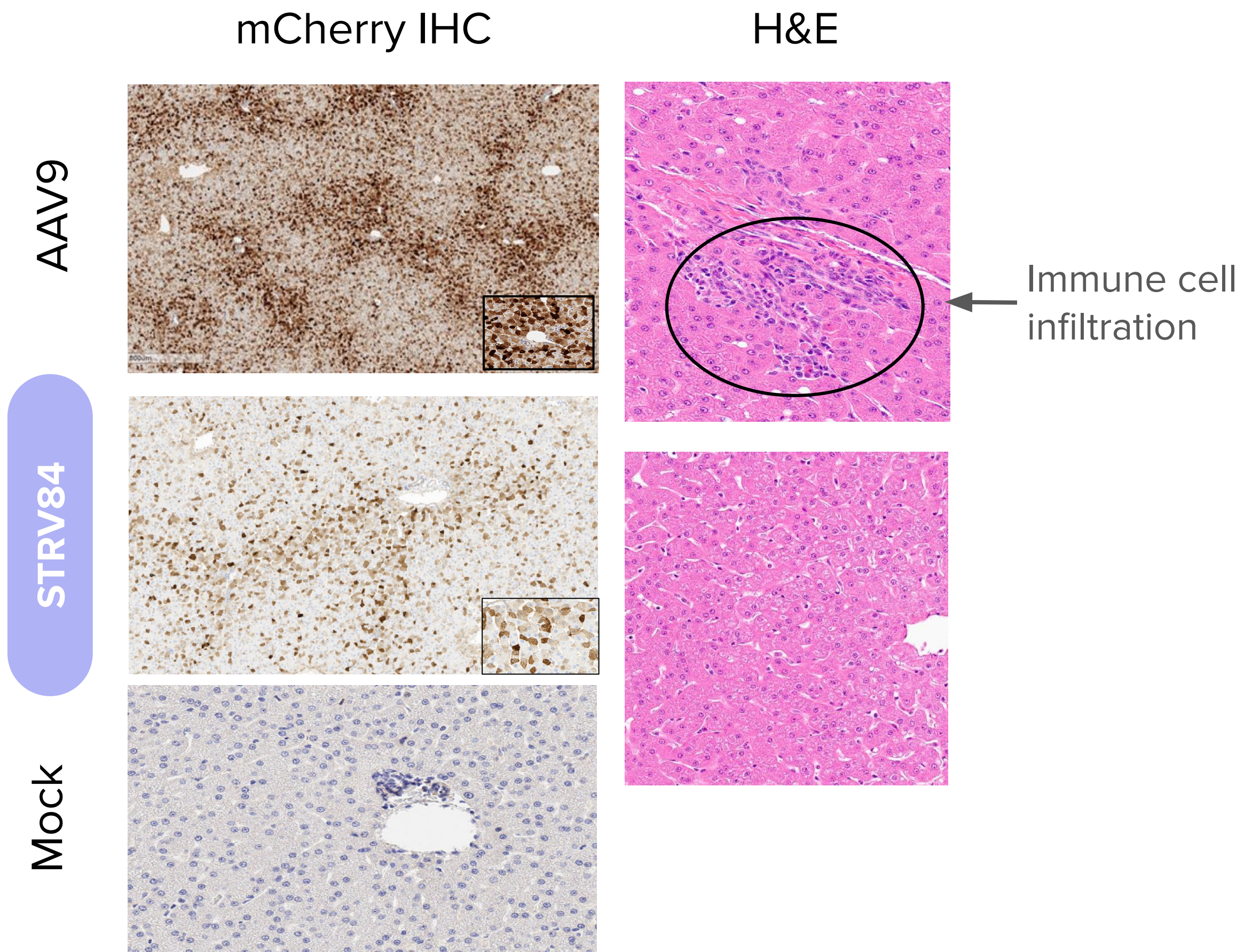


Enhanced potency of STRV84 vs. AAV9 in pigs

STRV84 exhibits increased potency in pig brain compared to AAV9 after IT administration and potency in pig spinal cord



Enhanced liver de-targeting of STRV84 vs. AAV9 in NHPs



mCherry Biodistribution in Liver

