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Systemic AAV vectors for widespread and targeted gene delivery in rodents

Rosemary C. Challis[1,3], Sripriya Ravindra Kumar[1,3], Ken Y. Chan[1], Collin Challis[1], Keith Beadle[1], Min J. Jang[1], Hyun Min Kim[1], Pradeep S. Rajendran[2], John D. Tompkins[2], Kalyanam Shivkumar[2], Benjamin E. Deverman[1] and Viviana Gradinaru[1*]

[1]Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, CA, USA. [2]Cardiac Arrhythmia Center and Neurocardiology Research Center of Excellence, University of California, Los Angeles, Los Angeles, CA, USA. [3]These authors contributed equally: Rosemary C. Challis and Sripriya Ravindra Kumar. *e-mail: viviana@caltech.edu

AAV-PHP capsid	Production	Species (strain or line), age injected	Organs/cell populations transduced	References
AAV-PHP.B	Good	Mouse (C57BL/6J and Cre driver lines), ≥6 weeks	Neurons, astrocytes, oligodendrocytes, and endothelial cells across all brain and spinal cord regions examined. Transduction in the retina occurs with variable efficiency across all layers	Ref. 1-3
		Mouse (C57BL/6J), P0-P1	Brain and spinal cord	Ref. 3
		Rat (Sprague-Dawley), P1 and 6 weeks	Neurons throughout the brain and spinal cord	Ref. 4
		Human iPSCs	Neurons and astrocytes in cortical spheroids	Ref. 2
AAV-PHP.eB	Good	Mouse (C57BL/6J, C57BL/6NCrl, FVB/NCrl, 129S1/SvImJ, 129T2/SvEmsJ, and Cre driver lines), ≥6 weeks	Similar to AAV-PHP.B but with increased efficiency of neuronal transduction	Ref. 5, this work
		Rat (Fischer), 6 weeks		
		Rat (Long Evans), 4 weeks		
		Rat (Sprague-Dawley), 6 weeks		Ref. 6
AAV-PHP.S	Good	Mouse (C57BL/6J and Cre driver lines), 6-8 weeks	Sensory neurons, peripheral ganglia (sympathetic, nodose, dorsal root, and cardiac ganglia), and the myenteric and submucosal plexus of the enteric nervous system. Robust transduction of heart muscle, skeletal muscle, and circular and longitudinal muscle of the digestive tract, as well as the liver and lungs	Ref. 5, this work
AAV-PHP.A	Poor	Mouse (C57BL/6J), 6 weeks	Astrocytes throughout the brain	Ref. 2

Supplementary Table 1. Use of AAV-PHP capsids for efficient transduction across specific organs and cell populations. Species/strains, organs, and cell populations examined to-date following intravenous administration of AAV-PHP viruses. To restrict gene expression to distinct cell types, use rAAV genomes with cell type-specific gene regulatory elements and/or Cre- or Flp-dependent recombination schemes (**Figs. 2-4** and **Table 1**).

Supplementary Table 2. Transfection calculator. This is an interactive calculator and provided as an Excel file (see Step 2 and REAGENT SETUP).

Volume of each step per gradient (ml)	Step		Number of gradients				
	%	Solution (ml)	1	2	4	6	8
6	15	DPBS + high salt	5.0	9.9	19.8	29.7	39.6
		60% iodixanol	1.7	3.3	6.6	9.9	13.2
6	25	DPBS + low salt	3.9	7.7	15.4	23.1	30.8
		60% iodixanol	2.8	5.5	11.0	16.5	22.0
		Phenol red	0.1	0.1	0.2	0.3	0.4
5	40	DPBS + low salt	1.8	3.7	7.3	11.0	14.7
		60% iodixanol	3.7	7.3	14.7	22.0	29.3
5	60	60% iodixanol	5.5	11.0	22.0	33.0	44.0
		Phenol red	0.1	0.1	0.2	0.3	0.4

Supplementary Table 3. Pouring the iodixanol density step solutions. Determine the number of gradients needed and prepare the iodixanol density step solutions (see REAGENT SETUP). The 15% step contains high salt to destabilize ionic interactions between viral particles and cell proteins in the clarified lysate[7]. In Step 16 (option B), prepare more step solution than is needed (see REAGENT SETUP).

Supplementary Table 4. Titration calculator. This is an interactive calculator and provided as an Excel file (see Step 42 and REAGENT SETUP).

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