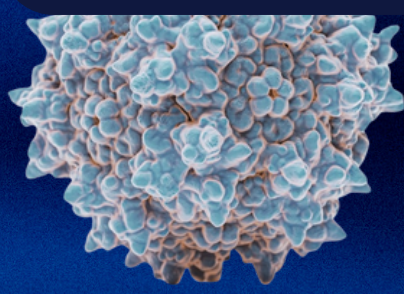
ATLANTIS BIOSCIENCE
Discovering Solutions

PackGene AAV
Packaging Services to Support Neuroscience Research



Adeno-associated virus (AAV), known for its low immunogenicity, high safety, and efficient gene delivery, has become essential in neuroscience research. It enables the delivery of exogenous genes to neurons, advancing studies in gene editing, optogenetics, and calcium imaging. AAV also introduces marker genes like fluorescent proteins, aiding in neuron tracing and subtype identification.

Applications of AAV in Neuroscience

Gene Function Studies

- Gene Editing → OE/shRNA/gRNA
  - Overexpression
    - Broad Spectrum: CAG, CBG, CMV, EF1a, miniCMV, EFS
    - Specific expression: hSyn, GFAP, CamKIIa, Iba1, TH, Mecp2
  - shRNA /gRNA
    - Knockdown: shRNA, mir30shRNA
    - Knockout: Cas9+gRNA, Cre/loxp

Neurophysiology or Neural Circuit Research

- Physiological Studies
  - Optogenetics
    - Activate: ChR2
    - Inhibit: eNpHR/ArchT
  - Chemogenetics
    - Activate: hM3d(Gq)
    - Inhibit: hM4d(Gl)
  - Calcium Indicators
    - GcamP6x/jGCaMP8x

General Steps in Neural Circuit Research

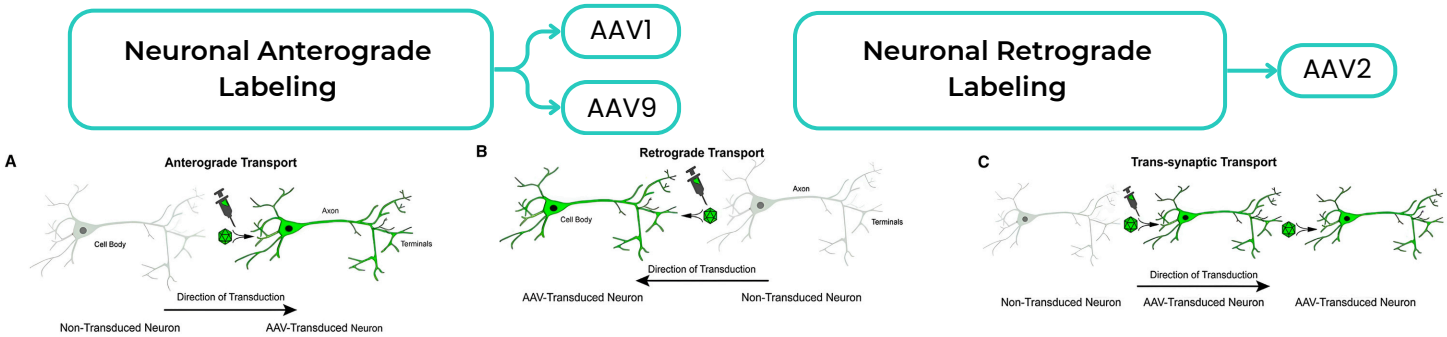
Investigating a specific behavior in an individual animal → Identification of key brainregions or neuron functions → Verification of key brain regions or neuron functions → Neural circuit tracing → Neural circuit functional verification

+65 8608 0974
www.atlantisbioscience.com
support@atlantisbioscience.com
Atlantis Bioscience Pte Ltd

How to Select AAV Serotypes for Neurological Research?

Neuronal Tracing Tools

Accurate labeling of neural circuits with AAV requires consideration of reversibility, including neuronal anterograde, and retrograde labeling.



Physical targeting of neuronal populations (Haggerty et al., 2020).

Serotypes that can cross the BBB

The existence of the blood-brain barrier (BBB) has a strong protective effect on the central nervous system (CNS), but it can also block the transmission and absorption of drugs. AAVPHP.B, AAVPHP.eB, and AAVPHP.S can effectively mediate the translocation of genes from the periphery to the CNS, and then deliver genetic material to the brain or spinal cord.

Serotypes	Validated Species	References
AAV-PHP.B	Mouse	PMID: 26829320
AAV-PHP.eB	Mouse	PMID: 28671695
AAV-PHP.S	Mouse	PMID: 28671695
AAV.CAP-B10	Mouse, Marmoset	PMID: 34887588
AAV.CAP-B22	Mouse, Marmoset	PMID: 34887588
MaCPNS1	Mouse, Rat, Rhesus macaque, Marmoset	PMID: 35643078
MaCPNS2	Mouse, Rat, Rhesus macaque, Marmoset	PMID: 35643078
AAV.CPP.16	Mouse, Cynomolgus macaque	PMID: 36217021
AAV.CAP-Mac	Marmoset, Rhesus macaque, Green monkey	PMID: 37430038
AAV-BI-hTFR1	Mouse	PMID: 38753766
PG008	Mouse	Developed by PackGene

Gene Manipulation Tools

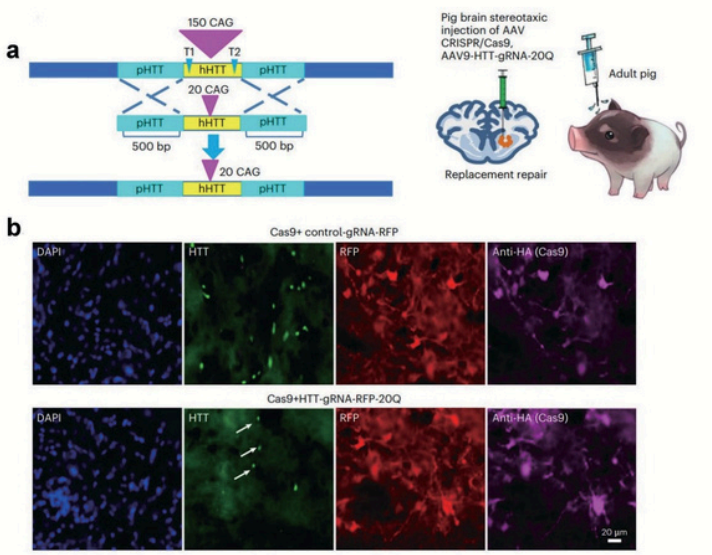
As a genetic manipulation tool, there are many serotypes that can be selected. Appropriate serotypes are often selected according to different parts of peripheral nerves, spinal cord, brain regions and cell types.

Area		Serotypes
Peripheral nervous system		AAVPHP.S, AAVrh10, AAV9
Spinal cord		AAVPHP.eB, AAVPHP.B, AAVrh10, AAV9, PG008
Brain	Whole brain	AAVPHP.eB, AAVPHP.B, AAV9, AAVrh10, PG008
Brain regions	Striatum	AAV5, AAV-DJ
	Hippocampus	AAV9, AAV-DJ, AAV2
	Cortex	AAV9, AAV8, AAV6, AAV5
	Substantia Nigra	AAV5
	Thalamus	AAV5
	Amygdala	AAV1, AAV6, AAV7, AAV8, AAV-DJ, AAVrh10

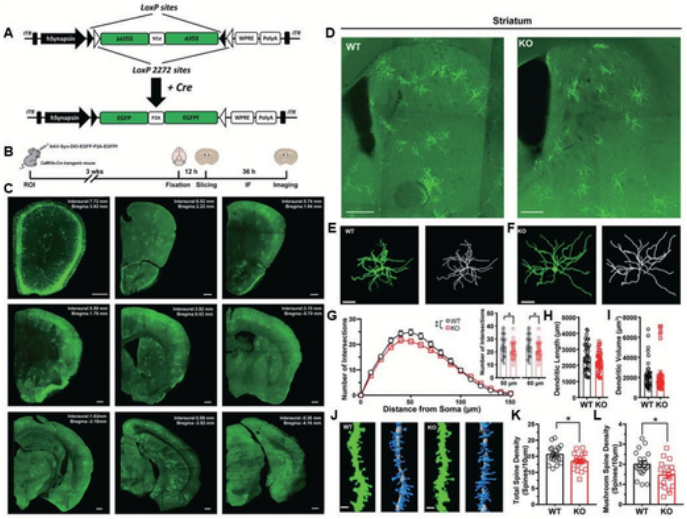
ATLANTIS BIOSCIENCE
Discovering Solutions

Case Study

	Gene Therapy for Huntington's Disease
Paper Title	Cas9-mediated replacement of expanded CAG repeats in a pig model of Huntington's disease
Journal	Nature Biomedical Engineering, 2023
Injection site	3-month-old pig striatum; neonatal pig auricular vein
Vector	AAV9-mini-cmv-spCas9; AAV9-control-gRNA-RFP; AAV9-HTT-gRNA-RFP-20Q
Serotype	rAAV9
Virus titer	3-5^12 vg/ mL
Injection volume	15 μL/side for 3-month-old pig; 500 μL for neonatal pig



	Cell-Type-Specific Sparse Neuron Labeling
Paper Title	A Whole-Brain Cell-Type-Specific Sparse Neuron Labeling Method and Its Application in a Shank3 Autistic Mouse Model
Journal	Frontiers in Cellular Neuroscience, 2020
Injection site	mouse retro-orbital sinus
Vector	AAV-PHP.eB-hSyn-DIO-EGFP-P2A-EGFP
Serotype	AAV-PHP.eB
Virus titer	1.3 × 10^12 vg/mL
Injection volume	100 μL



[1].The Lancet.(IF=98.4). Jun Lv, H.W.X.C., Z.W.B.Z. Jinghan Wang and R.C.Z.C. WuqingWang, AAV1-hOTOF genetherapy for autosomal recessive deafness 9-a single-arm trial. TheLancet, 2024. 403(10441): p. 2317-2325.

[2].Signal Transduct Target Ther. (IF=39.3).Shi, X., et al., LDL receptor-related protein 1 (LRP1),a novel target for opening the blood-labyrinth barrier (BLB). Signal Transduct Target Ther, 2022.7(1): p. 175.

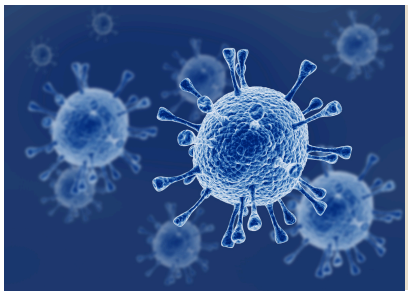
[3].Signal Transduct Target Ther. (IF=39.3).Tu, Z., et al., Tauopathy promotes spinal cord-dependent production of toxic amyloid-beta in transgenic monkeys. Signal Transduct TargetTher,2023. 8(1): p. 358.

[4].Nature biomedical engineering. (IF=28.1). Yan, S., et al., Cas9-mediated replacement ofexpanded CAG repeats in a pig model of Huntington's disease. Nature biomedical engineering,2023. 7(5): p. 629-646.

[5].Nature biomedical engineering. (IF=28.1). Alves, C.R.R., et al., Optimization of base editorsfor the functional correction of SMN2 as a treatment for spinal muscular atrophy. Nature biomedicalengineering, 2024. 8(2): p. 118-131

ATLANTIS BIOSCIENCE
Discovering Solutions

AAV Services at PackGene Biotech

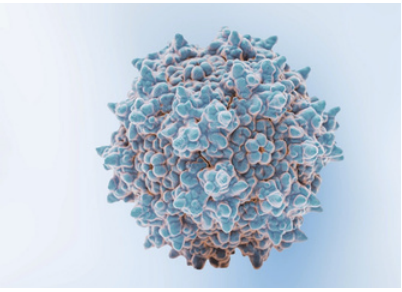


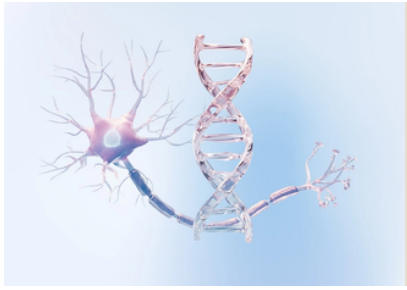
Vector Design and Construction

Packgene's online **piVector designer** can assist in the design and customization of AAV vectors for specific research applications. The team of experts can help optimize vector constructs for optimal transduction efficiency and expression levels in neural tissues.

AAV Production

We offer high-quality AAV vector production services for the delivery of genetic material to neuronal cells. We offer research grade, NHP grade and GMP grade AAV packaging services.





Off-the-shelf AAV

Fluorescent protein reporter-rAAV, Optogenetic-rAAV, Chemogenetic-rAAV, Cre -rAAV., et al.

Why Choose Us as your AAV Partner

Fast Turnaround
6-9 business days for AAV 5E+13GC

Guaranteed Titer
≥1E+13GC/mL (qPCR genome copies/mL)

High Yield
up to 1E+16 GC

High Quality
Purity: ≥95%, analyzed by SDS-PAGE; Endotoxin:<10EU/ml, suitable for in vivo experiments

Multiple Serotypes
80+ different serotype options available

+65 8608 0974
www.atlantisbioscience.com
support@atlantisbioscience.com
Atlantis Bioscience Pte Ltd

In the field of neurological disease applications, we provide AAVs for fluorescent controls, CRISPR, optogenetics, calcium indicators, Cre recombinase, and Neurological disease modeling.

Product Classification	Promoter Type	Plasmid Number	Plasmid Name
Fluorescence control	Universal promoter	EA021	ssAAV.CAG.EGFP.WPRE.SV40pA
		EC021	scAAV.CAG.EGFP.WPRE.SV40pA
		EA041	ssAAV.CMV.EGFP.WPRE.SV40pA
		EC041	scAAV.CMV.EGFP.WPRE.SV40pA
		EA022	ssAAV.CAG.mCherry.WPRE.SV40pA
		EA031	ssAAV.EF1a.EGFP.WPRE.SV40pA
		EA026	ssAAV.CAG.EYFP.WPRE.SV40pA
	Tissue-specific promoter	EC101	scAAV.hSyn.EGFP.WPRE.SV40pA
		EA171	ssAAV.hGFAP5.EGFP.WPRE.SV40pA
		EA102	ssAAV.hSyn.mCherry.WPRE.SV40pA
		EA501	ssAAV.Iba1.EGFP.WPRE.SV40pA
Cre	CAG	NX022	sssAAV.CAG.EGFP-2A-Cre.WPREs
	CMV	NX043	ssAAV.CMV.mCherry-2A-Cre.WPRE.SV40pA
		NX041	ssAAV.CMV.optCre.WPRE.SV40pA
	hSyn	NX101	ssAAV.hSyn.optCre.WPREs
		NX102	ssAAV.hSyn.EGFP-2A-Cre.WPREs
	cTNT	NX182	ssAAV.cTNT.EGFP-2A-Cre.WPREs.SV40pA
	CaMKIIa	NX133	ssAAV.CaMKIIa.mCherry-2A-Cre.WPRE.SV40pA
Optogenetics	EF1a	OT031	ssAAV.EF1a-double floxed-EYFP
		OT035	ssAAV.EF1a-eNpHR 3.0-EYFP
		OT037	ssAAV.EF1a-ChR2-mCherry
	CaMKIIa	OT135	ssAAV.CaMKIIa-eNpHR 3.0-EYFP
		OT137	ssAAV.CaMKIIa-ChR2-mCherry
	GFAP	OT174	ssAAV.GFAP-DIO-eNpHR 3.0-EYFP
		OT175	ssAAV.GFAP-eNpHR 3.0-EYFP
		OT179	ssAAV.GFAP104-DIO CIV1 (tt)-TS-mCherry
Chemogenetics	EF1a	DR032	ssAAV.EF1a-DIO-HA-hM3D(Gq)-IRES-mCitrine
		DR035	ssAAV.EF1a-hM3D(Gq)-mCherry
		DR036	ssAAV.EF1a-DIO-hM3D(Gq)-mCherry
		DR039	ssAAV.EF1a-DIO-hM4D(Gi)-mCherry
		DR313	ssAAV.EF1a-HA-KORD-IRES-mCitrine
		DR314	ssAAV.EF1a-DIO-GFP
	mOXT	DR391	ssAAV.mOXT-hM3Dq-mCherry-WPRE
		DR392	ssAAV.mOXT-DIO-HA-hM3D(Gq)-IRES-mCitrine
		DR394	ssAAV.mOXT-HA-hM3D(Gq)-mCherry
		DR396	ssAAV.mOXT-DIO-hM3D(Gq)-mCherry
		DR398	ssAAV.mOXT-DIO-hM3D(Gs)-mCherry
		DR3912	ssAAV.mOXT-dF-HA-KORD-IRES-mCitrine
		DR3913	ssAAV.mOXT-HA-KORD-IRES-mCitrine

Product Classification	Promoter Type	Plasmid Number	Plasmid Name
Chemogenetics	hSyn	DR101	ssAAV.hSyn-hM3Dq-mCherry-WPRE
		DR103	ssAAV.hSyn-HA-hM3D(Gq)-IRES-mCitrine
		DR106	ssAAV.hSyn-DIO-hM3D(Gq)-mCherry
		DR108	ssAAV.hSyn-DIO-hM3D(Gs)-mCherry
		DR109	ssAAV.hSyn-DIO-hM4D(Gi)-mCherry
		DR1014	ssAAV.hSyn.DIO.EGFP.WPRE.bGHpA
	CaMKIIa	DR131	ssAAV.CaMKIIa-hM3Dq-mCherry-WPRE
		DR133	ssAAV.CaMKIIa-HA-hM3D(Gq)-IRES-mCitrine
		DR134	ssAAV.CaMKIIa-HA-hM3D(Gq)-mCherry
		DR135	ssAAV.CaMKIIa-hM3D(Gq)-mCherry
		DR138	ssAAV.CaMKIIa-DIO-hM3D(Gs)-mCherry
		DR139	ssAAV.CaMKIIa-DIO-hM4D(Gi)-mCherry
		DR310	ssAAV.CaMKIIa-HA-hM4D(Gi)-mCherry
CRISPR/Cas9	Universal promoter	XA20	ssAAV.miniCMV.SpCas9
		XA02	ssAAV.EFS.SpCas9
		XB02	ssAAV.EFS.SpCas9HF
		XB06	ssAAV.miniCMV.SpCas9HF
		AC010	ssAAV.EFS.SaCas9
		AC040	ssAAV.CMV.SaCas9
		AD010	ssAAV.EFS.SaCas9HF
		AC050	ssAAV.TBG.SaCas9
	Tissue-specific promoter	AC090	ssAAV.hDesmin.SaCas9
		AC100	ssAAV.hSynapsin.SaCas9
		AC120	ssAAV.pMECP2.SaCas9
		AC091	ssAAV.hDesmin.SaCas9.U6.(Sa)sgRNA
		AC101	ssAAV.hSynapsin.SaCas9.U6.(Sa)sgRNA
		AC121	ssAAV.pMECP2.SaCas9.U6.(Sa)sgRNA
		AD060	ssAAV.Elastasel.SaCas9HF
		AD070	ssAAV.rInsulin2.SaCas9HF
		AD080	ssAAV.rInsulin2.SaCas9HF
		AD090	ssAAV.hDesmin.SaCas9HF
		AD100	ssAAV.hSynapsin.SaCas9HF
		AD120	ssAAV.MECP2.SaCas9HF
Neurological disease modeling	Parkinson's disease (PD)	pSS042	ssAAV.CaMKIIa.hSNCA(A53T)-P2A-mScarlet.WPRE.SV40pA
		pSS043	ssAAV.hSyn-GFP-IRES-hSNCA(A30P)
		pSS044	ssAAV.hSyn-GFP-IRES-hSNCA
	Alzheimer's disease (AD)	pDSS016	ssAAV-CAG-tau(p301L)-WPRE-bGHpA
		pSS045	ssAAV-CAG-APPSL-WPRE-bGHpA
		pDSS015	ssAAV-CAG-PS1-M146L-WPRE-bGHpA
	Amyotrophic lateral sclerosis (ALS)	pSS046	ssAAV-SYN-TDP-43-WPRE-bGHpA
		pSS047	ssAAV-SYN-TDP-43(M337V)-WPRE-bGHpA