Petrovsky National Research Center of Surgery

SECHENOV UNIVERSITY

XXXII Symposium on Bioinformatics and Computer-Aided Drug Discovery (BCADD-2026)



COMPARATIVE EXPERIMENTAL AND COMPUTATIONAL ANALYSIS OF AAV9 AND AAVRH.10 TRANSPORT ACROSS THE BLOOD–BRAIN BARRIER

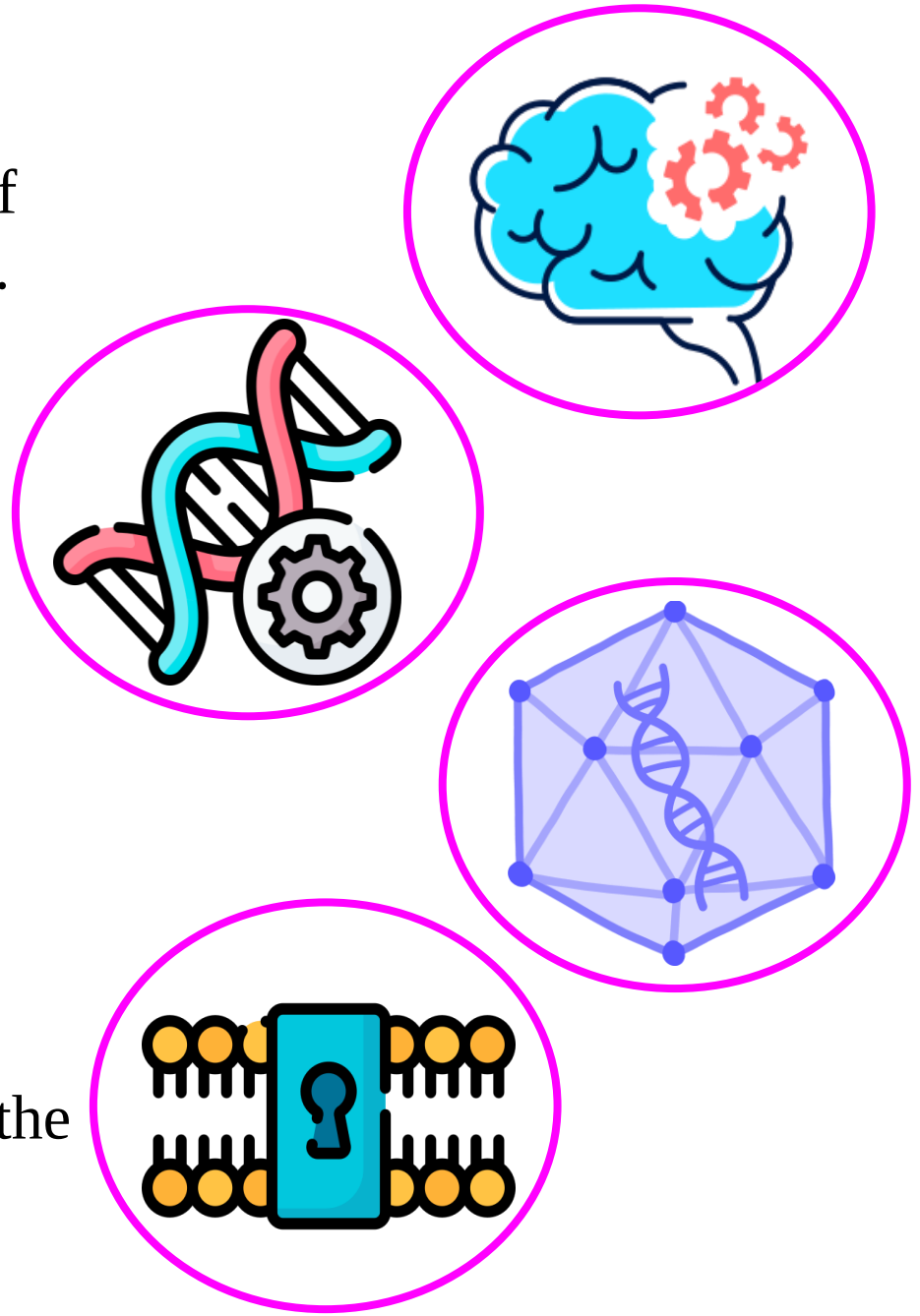
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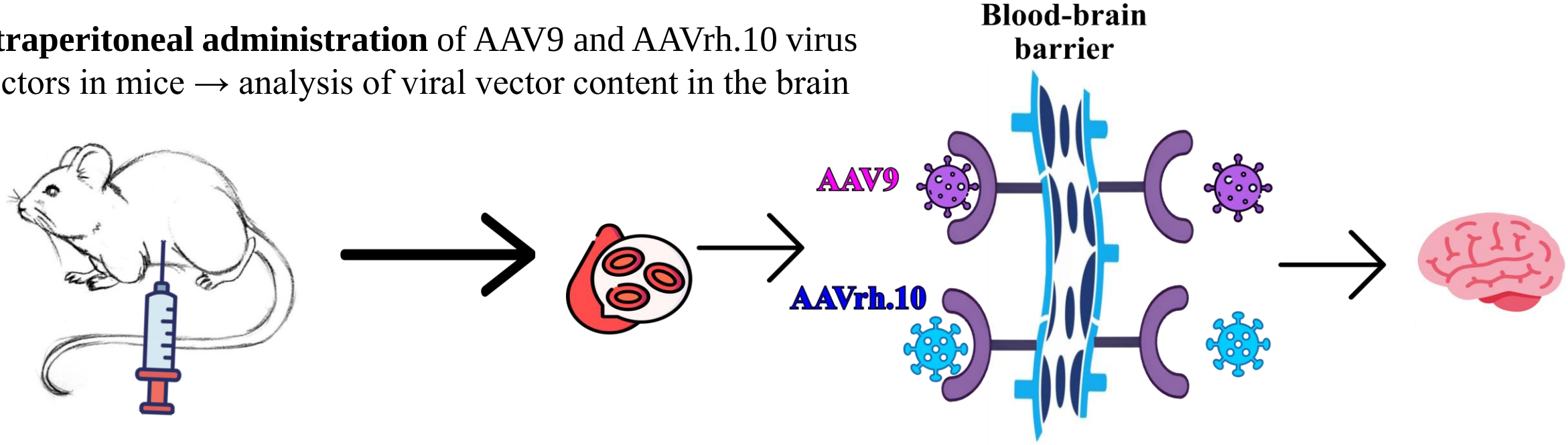
2026

Gene therapy for neurological disorders

- Neurological diseases are difficult to treat; the presence of the **blood-brain barrier** presents an additional challenge.
- Gene therapy using **adeno-associated viruses (AAVs)** is considered a promising approach to treat neurological diseases
- **AAV9 and AAVrh.10**:
  - ✓ have neuronal tropism
  - ✓ can cross blood-brain barrier
  - ✓ have the ability to move along axons, ensuring widespread dissemination
- The process of AAV cell entry is complex and involves multiple stages. The protein KIAA0319L, also known as the **AAVR**, is believed to **play a key role** in this process for several serotypes, including AAV9 and AAVrh.10



Intraperitoneal administration of AAV9 and AAVrh.10 virus vectors in mice → analysis of viral vector content in the brain



System preparation (use experimentally determined 3D structures from Protein Data Bank) → Energy Minimization, Structure Refinement → Molecular Docking (HADDOCK) → Molecular Dynamics (triplet)

Creating complexes of AAV9-AAVR and AAVrh.10-AAVR

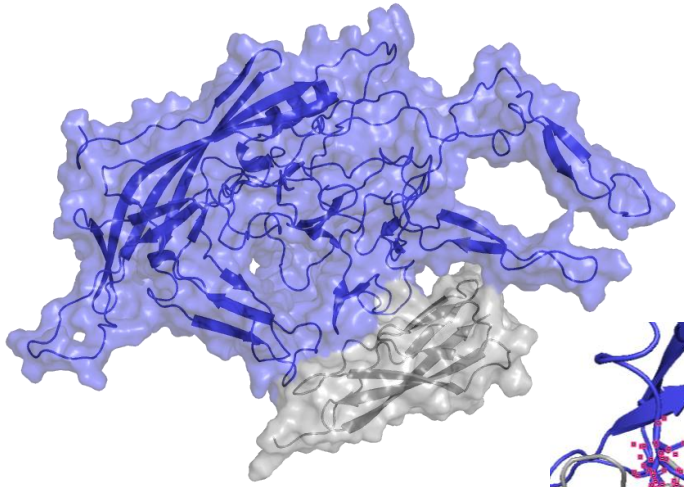
Experimentally determined 3D structures :

✓ Whole capsomers of both AAV9 and AAVrh.10

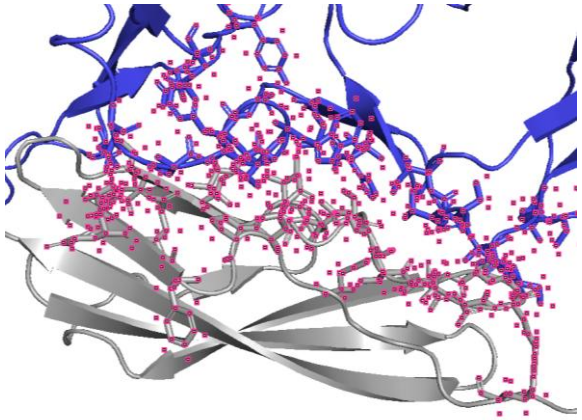
× Whole AAVR → only a fragment

✓ AAVR in complex with AAV9

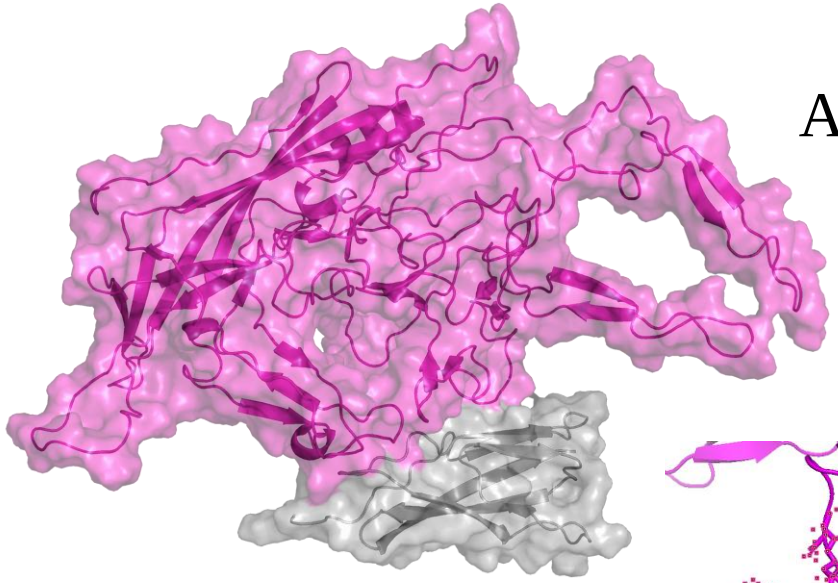
× AAVR in complex with AAVrh.10 → no



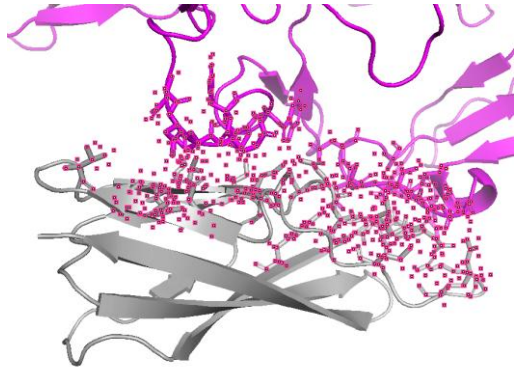
AAVrh.10 VP1



AAVR



AAV9 VP1



AAVR

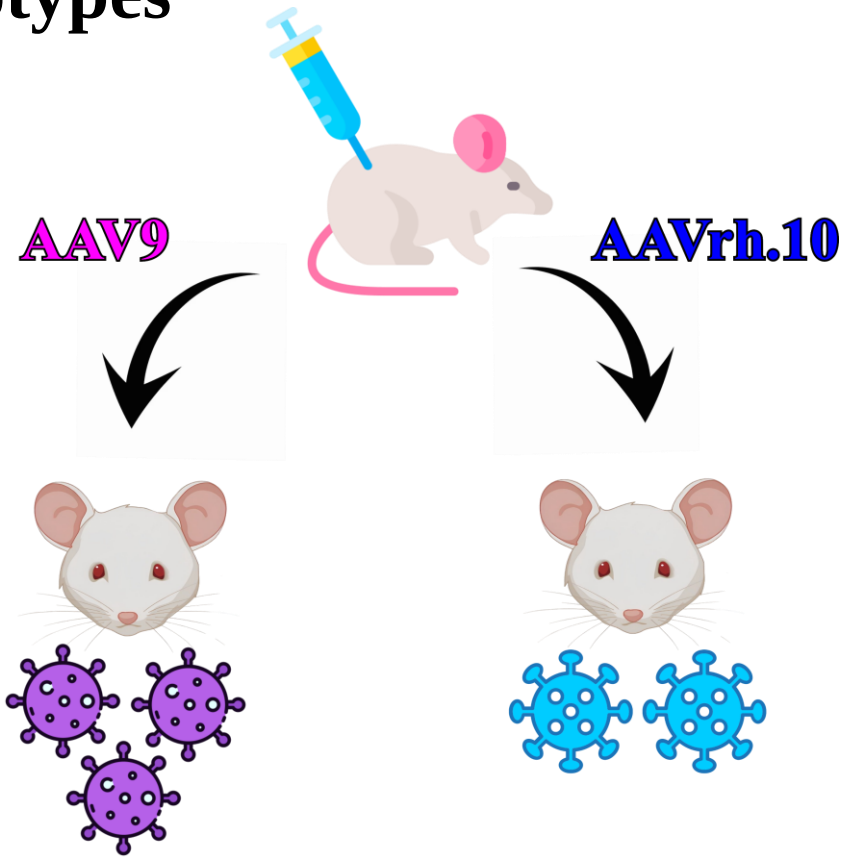
Solution:

- Use experimentally determined 3D structure of complex AAV9 VP1 protein in complex with AAVR fragment as a template to create an analogous complex for AAVrh.10. VP1 proteins of AAV9 and AAVrh.10 are 84% similar according to BLAST.

Result: AAVR recognition contributes to the distinct BBB transport efficiencies of AAV9 and AAVrh.10 serotypes

Experimental evaluation revealed a higher BBB permeability for AAV9 compared to AAVrh.10.

AAV9		AAVrh.10
+ + +	In vivo experiment	+ +
+ + +	FoldX	+ +
+ + +	HADDOCK	+ +
+ + +	MD	+ +



Computational analysis was consistent with experimental observations

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