

Passive Amylin Immunotherapy Improves Brain Function and Reduces Brain β -amyloid Pathology in APP/PS1 Mice

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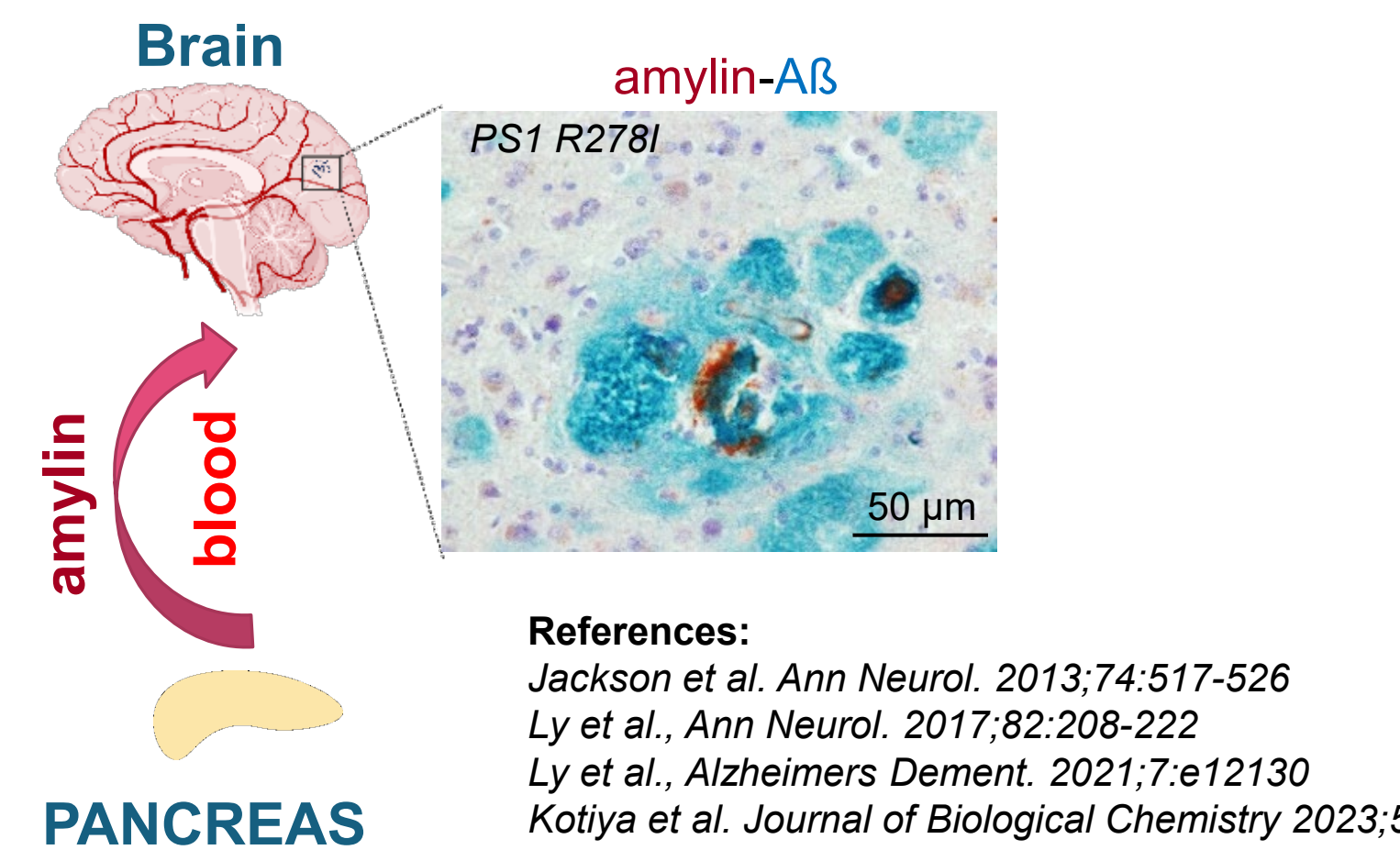
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Introduction

□ Amylin is a systemic hormone that is co-secreted with insulin from pancreatic β -cells. Amylin co-aggregates with brain parenchymal and vascular β -amyloid in persons with Alzheimer's dementia.

□ The present study investigates whether passive amylin immunotherapy using a polyclonal anti-amylin antibody (P2) can reduce amylin transport across the Blood-Brain-Barrier (BBB), suppress downstream tau-phosphorylating signaling pathways, and improve pathological outcomes in AD models.



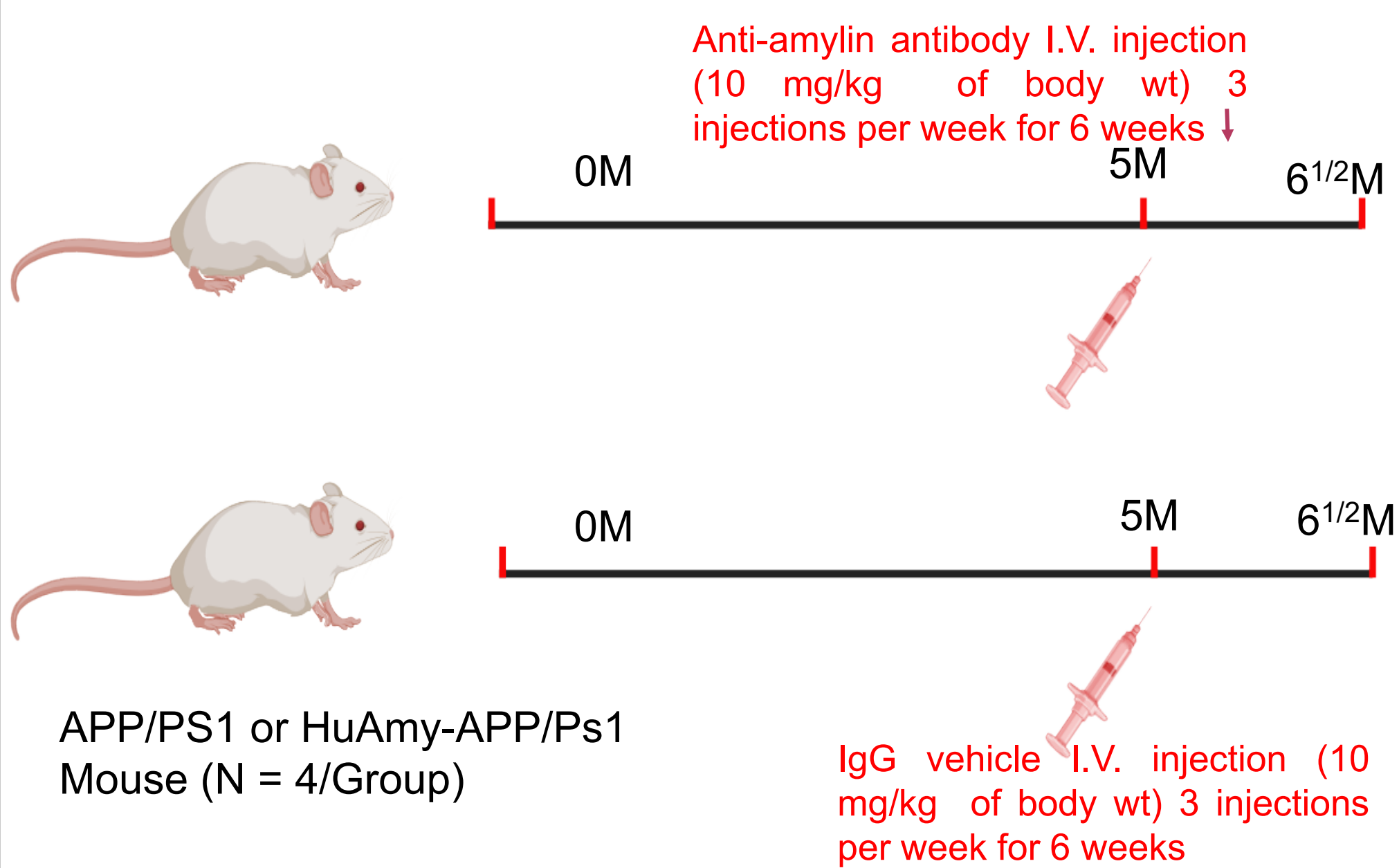
Method

□ We have generated a polyclonal anti-amylin antibody (P2) in rabbits using the N-terminal of amylin peptide as an immunogen.

□ Five-month-old male APP/PS1 mice and APP/PS1 mice expressing human amylin (HuAmy-APP/PS1) were randomized to receive rabbit IgG or P2 (10 mg/kg, i.v., three times/week for 6 weeks; n=8-9/group).

□ Animals were assessed for adverse effects, novel object recognition (NOR), body weight, and blood glucose. P2 levels were quantified in plasma, brain, and kidney. Hippocampal A β and pS214 Tau was measured by ELISA, and vascular integrity was assessed by H&E and Prussian blue staining.

□ To define (BBB) and signaling mechanisms, a rat 3D endothelial-astrocyte co-culture BBB model was used to assess FAM-amylin transcytosis, TEER (Trans-Endothelial-Electrical-Resistance), Endothelial cAMP levels, and PKA activation.



Contact Information

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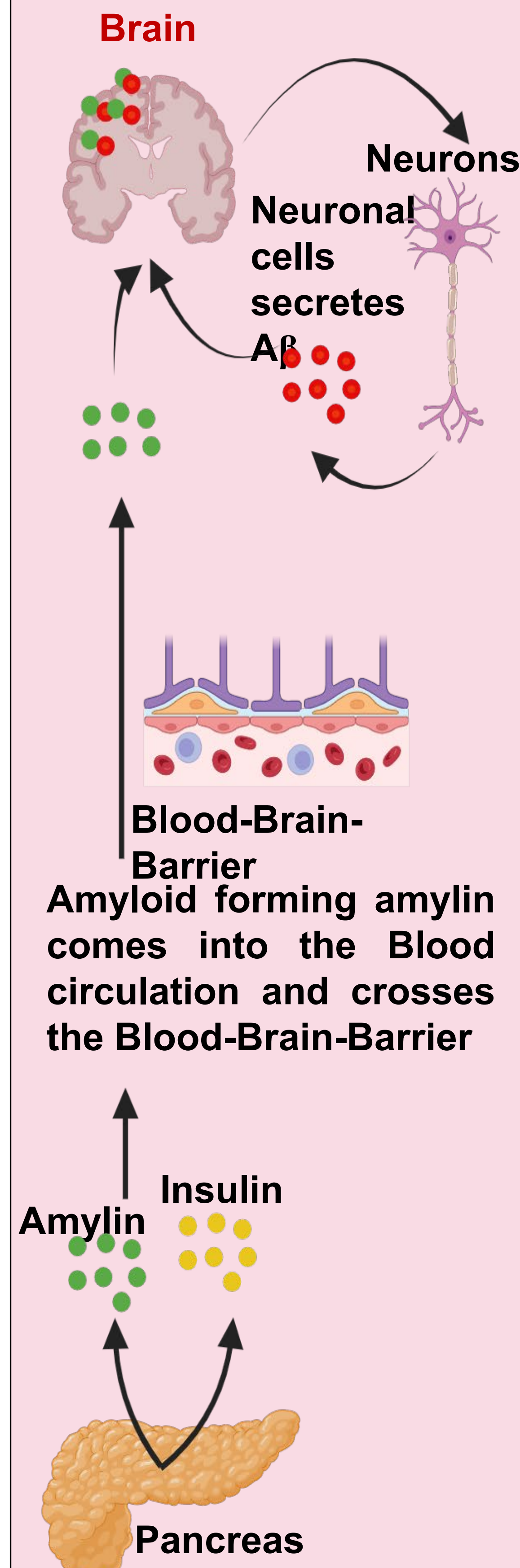
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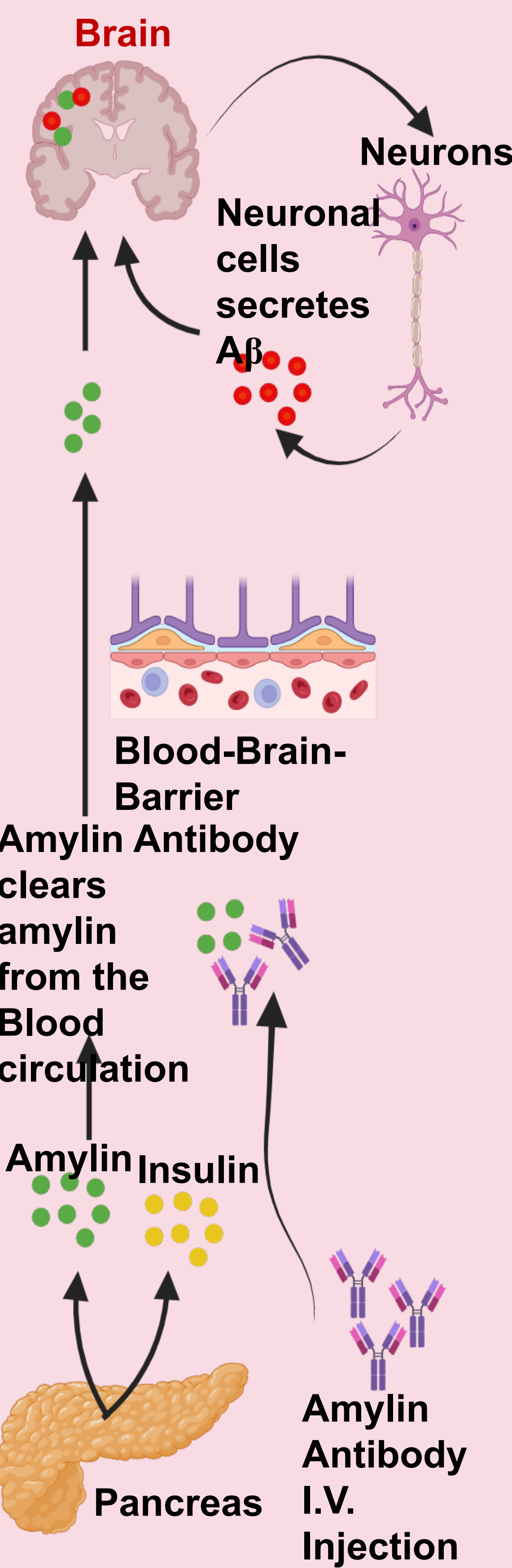
Pathological condition

Increased A β -amyloid deposition in brain and impaired brain function



Passive Amylin Immunotherapy

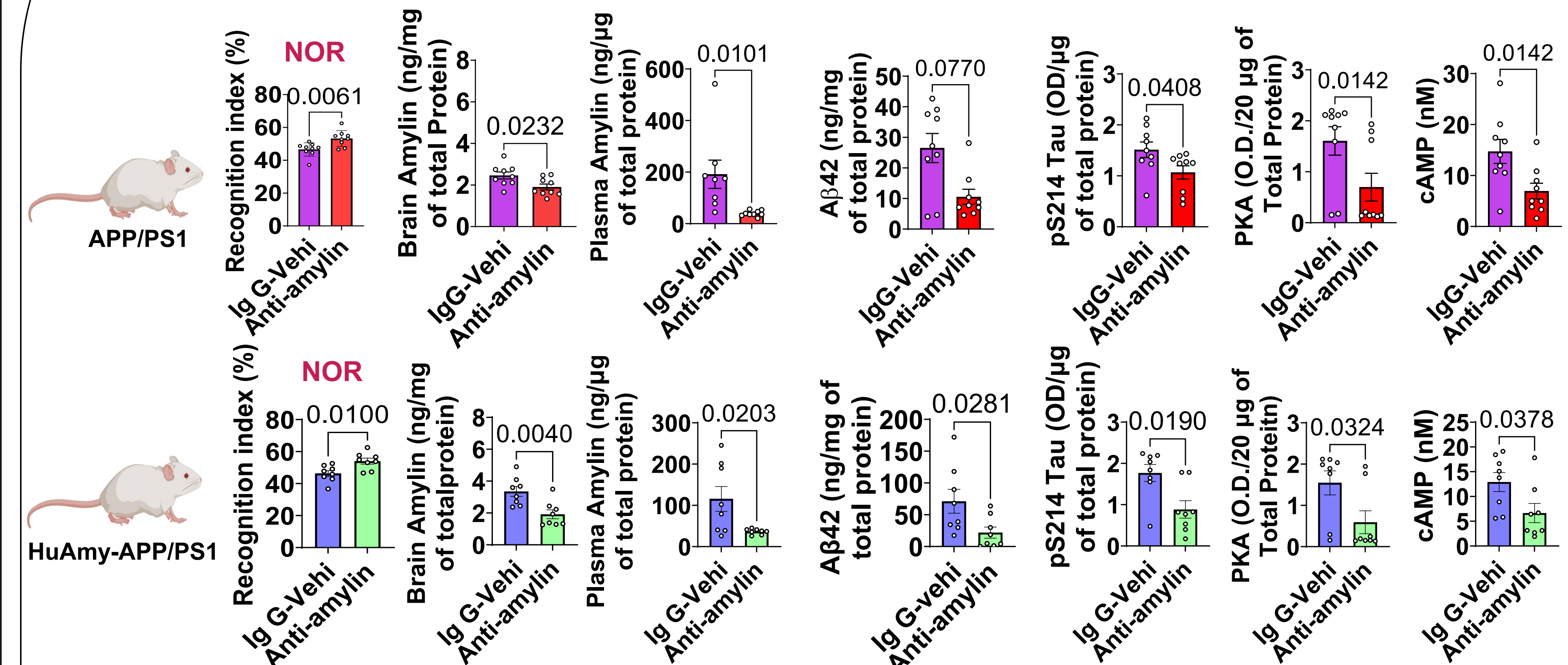
Decreased A β -amyloid deposition in brain and improved brain function



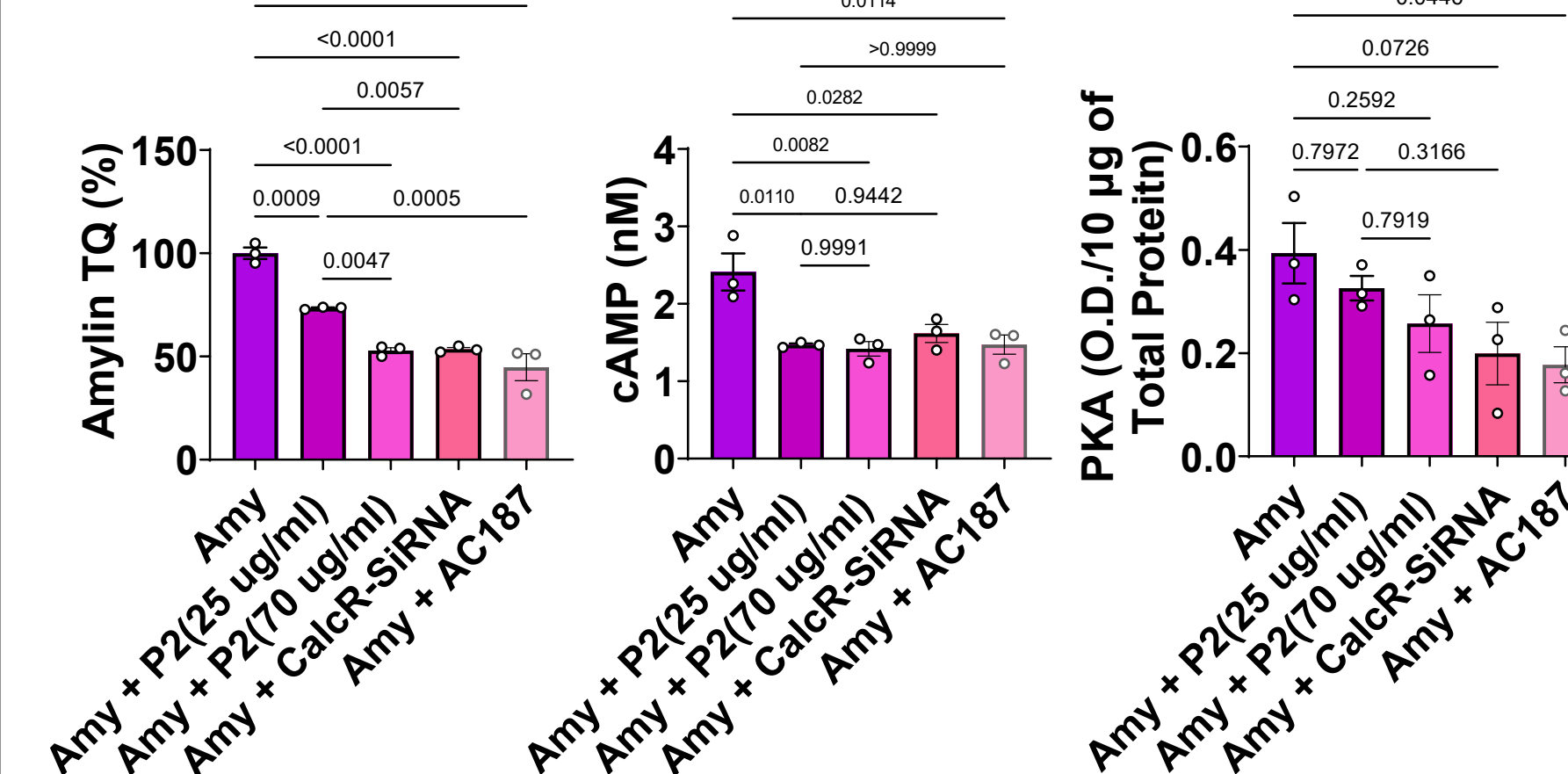
Under pathological conditions, amyloid-forming amylin crosses the blood-brain barrier and interacts with A β , promoting A β -amyloid deposition in the brain and impairing brain function. Passive amylin immunotherapy, administered via intravenous injection, clears amyloid-forming amylin from the blood circulation, resulting to reduced A β -amyloid deposition in the brain and improved cognitive function..

Results

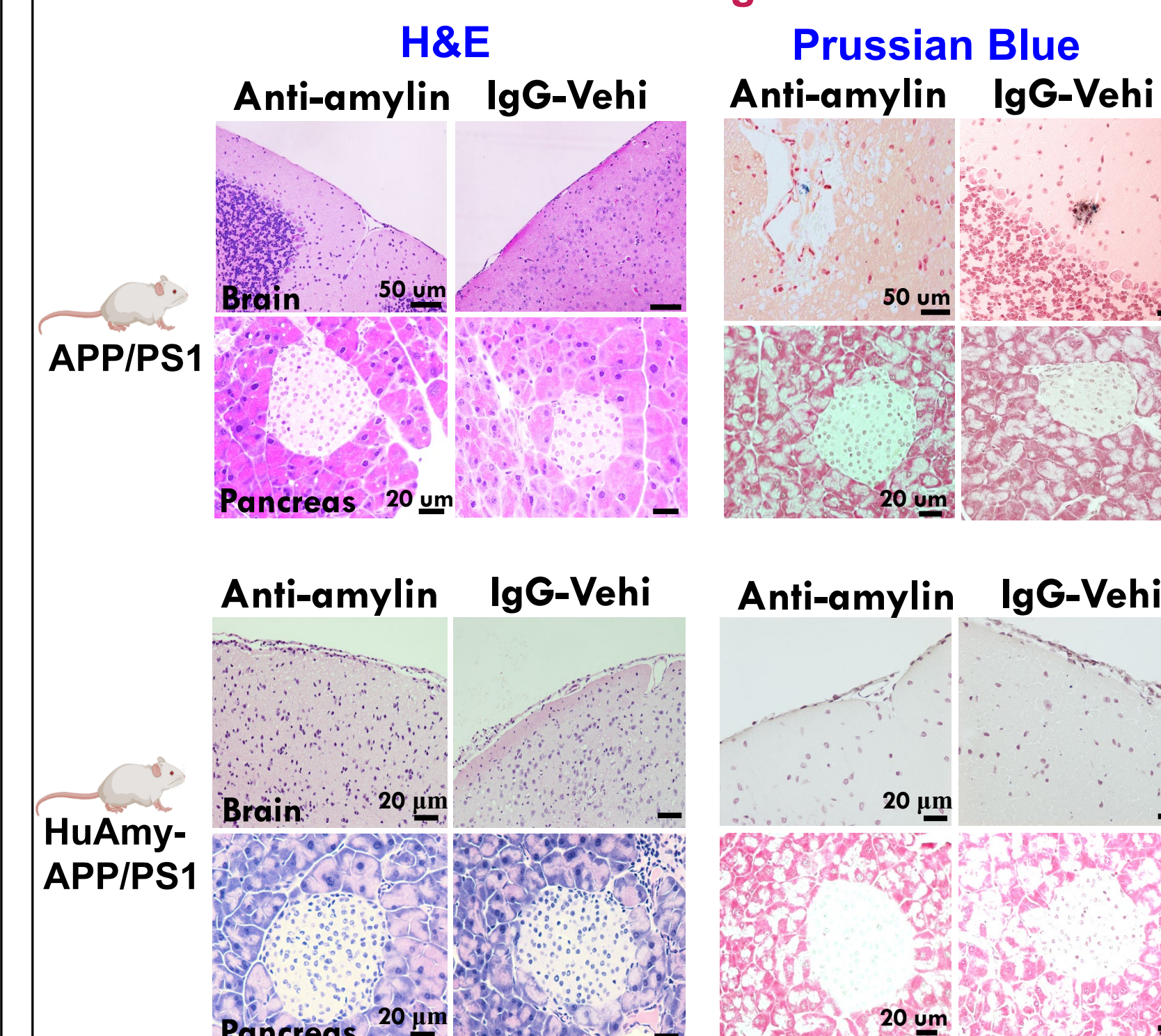
NOR and Level of Brain & Plasma Amylin, Brain A β -42, pS214 Tau, cAMP and PKA Activity in AD Mouse Model



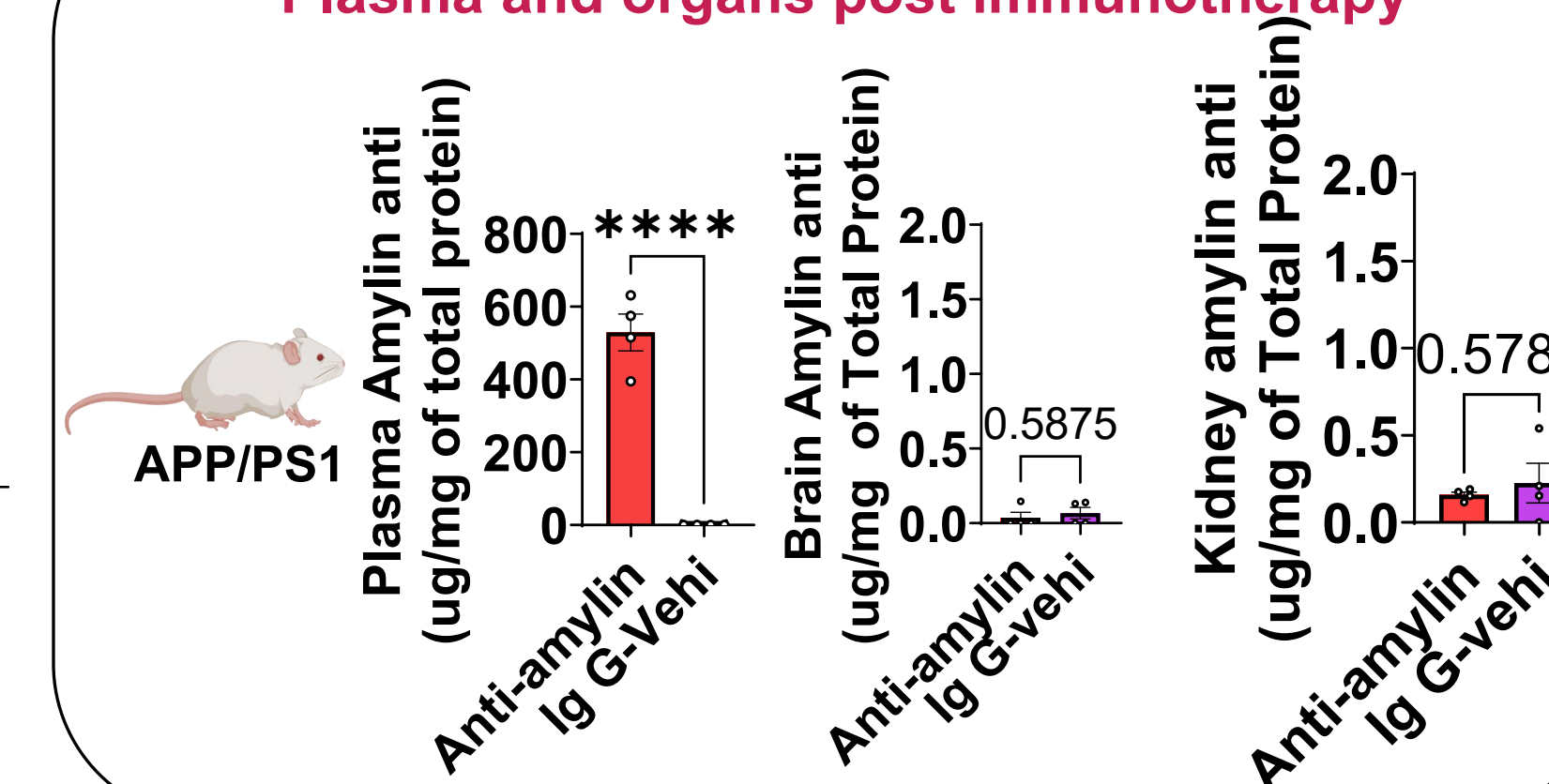
Rat 3D Endothelial-Astrocyte Co-Culture BBB Model



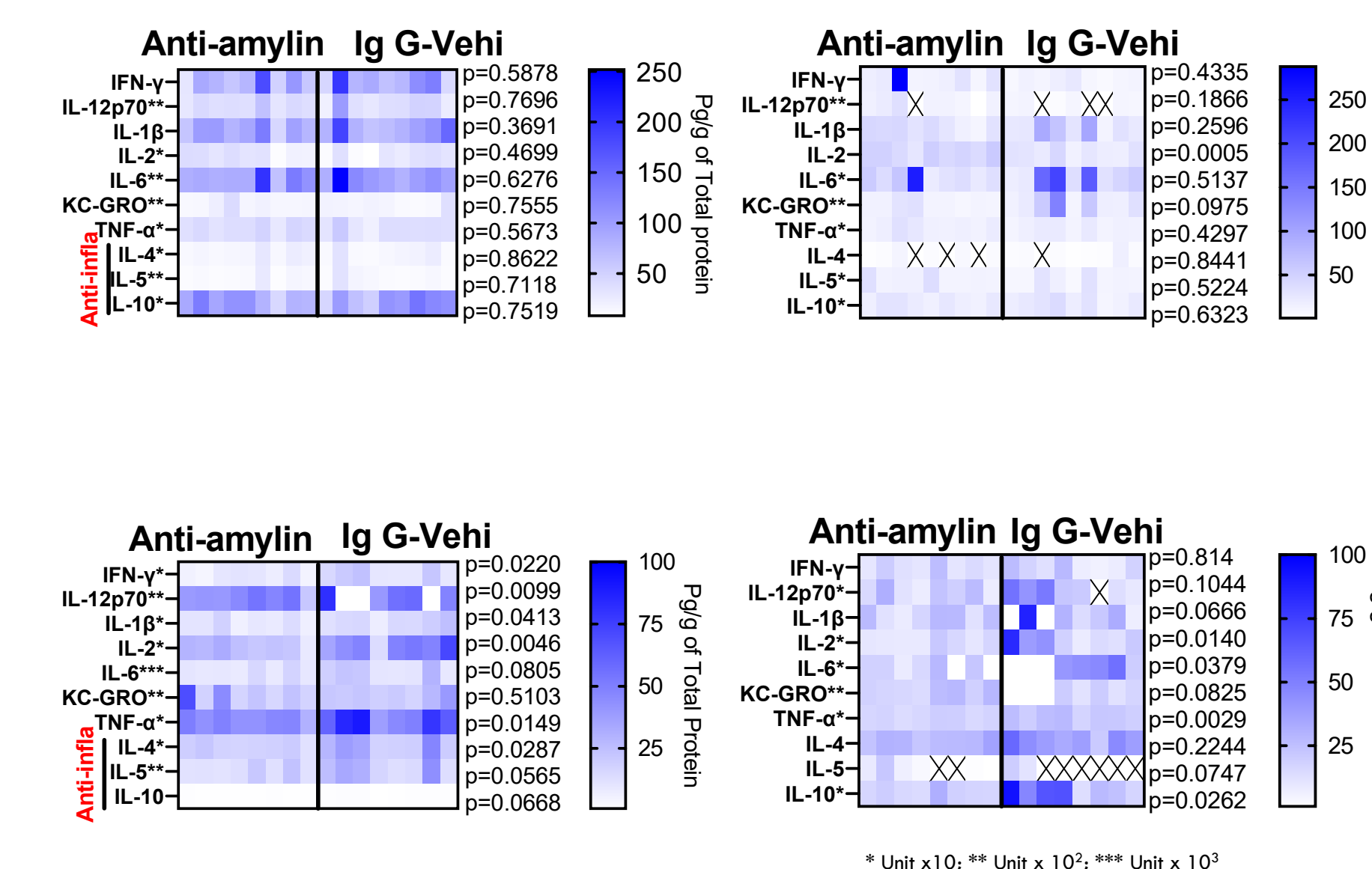
H&E and Prussian Blue Staining in Brain and Pancreas



Detection of injected Amylin Antibody (P2) in Plasma and organs post immunotherapy



Level of Cytokines in Brain and Plasma



Conclusion

- ✓ Passive amylin immunotherapy safely neutralizes circulating amyloid-forming amylin, limits its BBB transport, and suppresses PKA-cAMP pathway of tau phosphorylation and A β pathology.
- ✓ These findings suggest a mechanistic link between peripheral amylin, neurovascular dysfunction, and tau pathology, supporting P2 as a possible disease-modifying therapeutic strategy for AD.