# Deciphering gut-to-brain α-synuclein propagation via PRV-based single-cell tracing

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**Abstract**

Recent studies have highlighted the importance of the gut-to-brain axis as a connective pathway in Parkinson's disease (PD). It has been suggested that misfolded α-synuclein (α-syn) aggregates in the gastrointestinal tract and propagate through the vagus nerve to the brainstem. To model the process, we injected the pseudorabies virus (PRV) near the stomach, which then traveled upstream to the medulla-pons along the gut-brain axis. Next, we performed single-nucleus RNA sequencing (snRNA-seq) on medulla–pons tissue following pseudorabies virus (PRV) retrograde tracing and identified the PRV+ (infected) neurons and compared them with the reference atlas of brainstem neurons. Differential expression analysis revealed that PRV+ neurons exhibited robust upregulation of several marker genes that are not found in the reference, supporting the notion that these neurons may capture receptor pathways relevant to α-syn propagation. Collectively, our findings provide molecular insight into how PRV+ neurons may contribute to the gut–brain spread of PD pathology.

**Keywords**: Gut–to-brain axis, vagus nerve, Parkinson's disease, α-synuclein propagation, single-nucleus RNA sequencing (snRNA-seq)