

Induction of Alzheimer pathology modulates transcriptomic profile in a non-human primate

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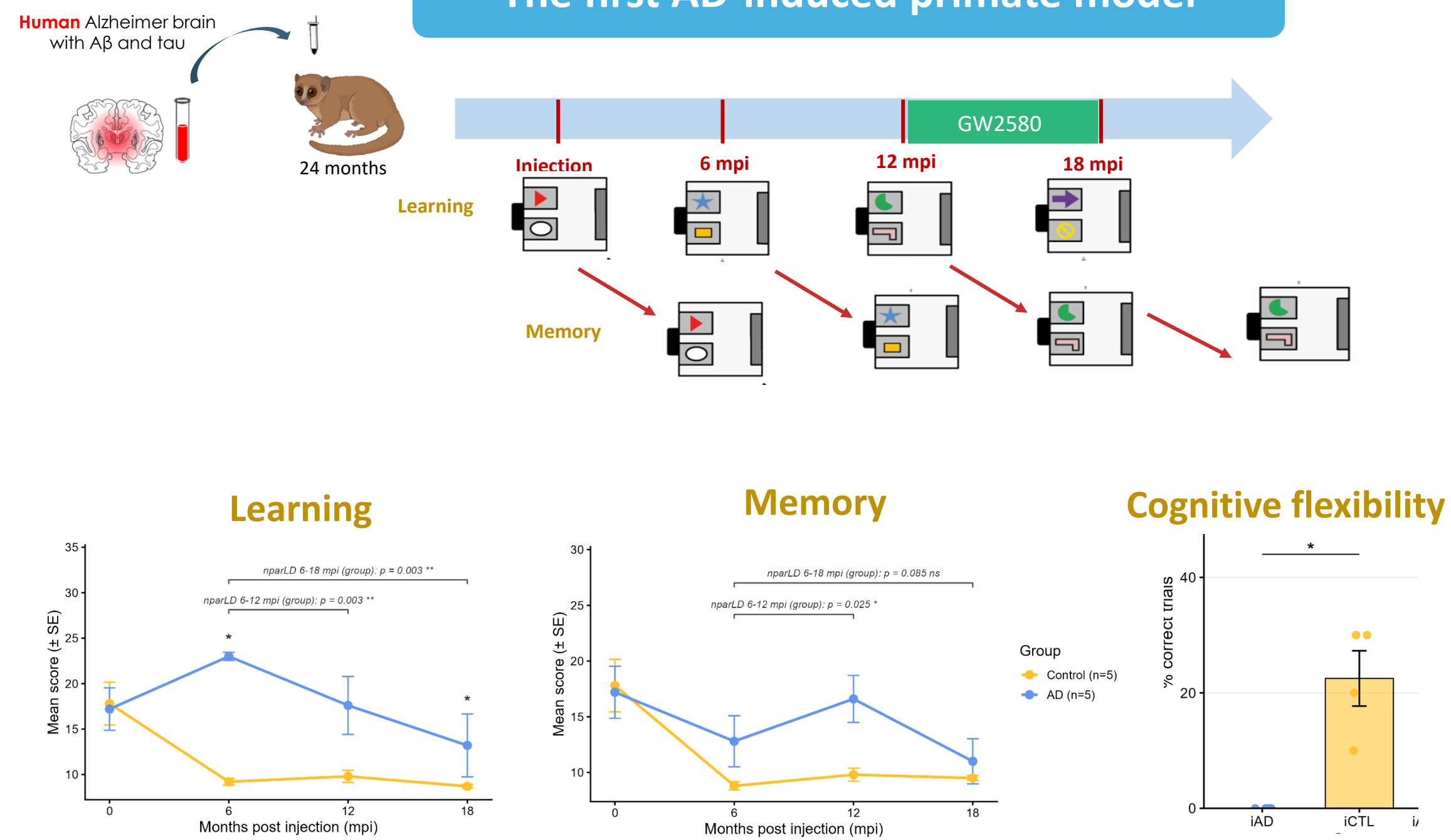
Introduction

- Understanding the early molecular events underlying Alzheimer's disease (AD) is essential for developing effective therapeutic strategies.
- Transcriptomic approaches, particularly unbiased data-driven analyses, provide powerful tools to identify these early molecular changes.
- Single-cell RNA sequencing (scRNA-seq) has uncovered the remarkable heterogeneity of microglia, including the identification of Disease-Associated Microglia (DAM) associated with AD progression (Keren-Shaul et al., 2017).
- However, most current transcriptomic knowledge is derived from transgenic mouse models, which fail to fully recapitulate sporadic AD and human microglial transcriptomic signatures (Boche et al., 2021).

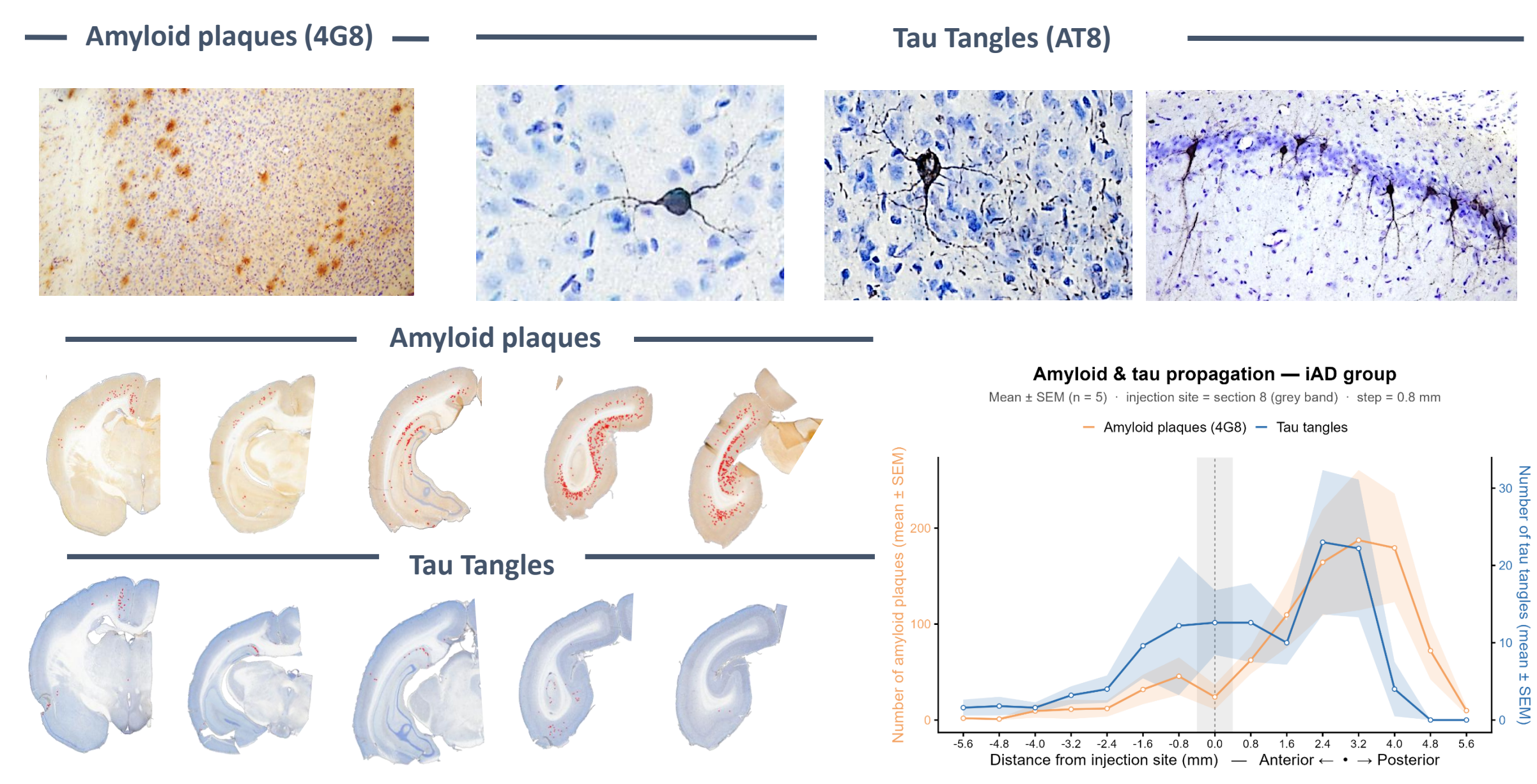


- Longevity (14 years)
- Phylogenetic proximity
- APP (Ab) and MAPT (tau) similar to human
- Amyloidosis and tauopathy spontaneously
- Inducible Alzheimer's disease model (Lam, 2021)
- Slow and early AD model

The first AD-induced primate model

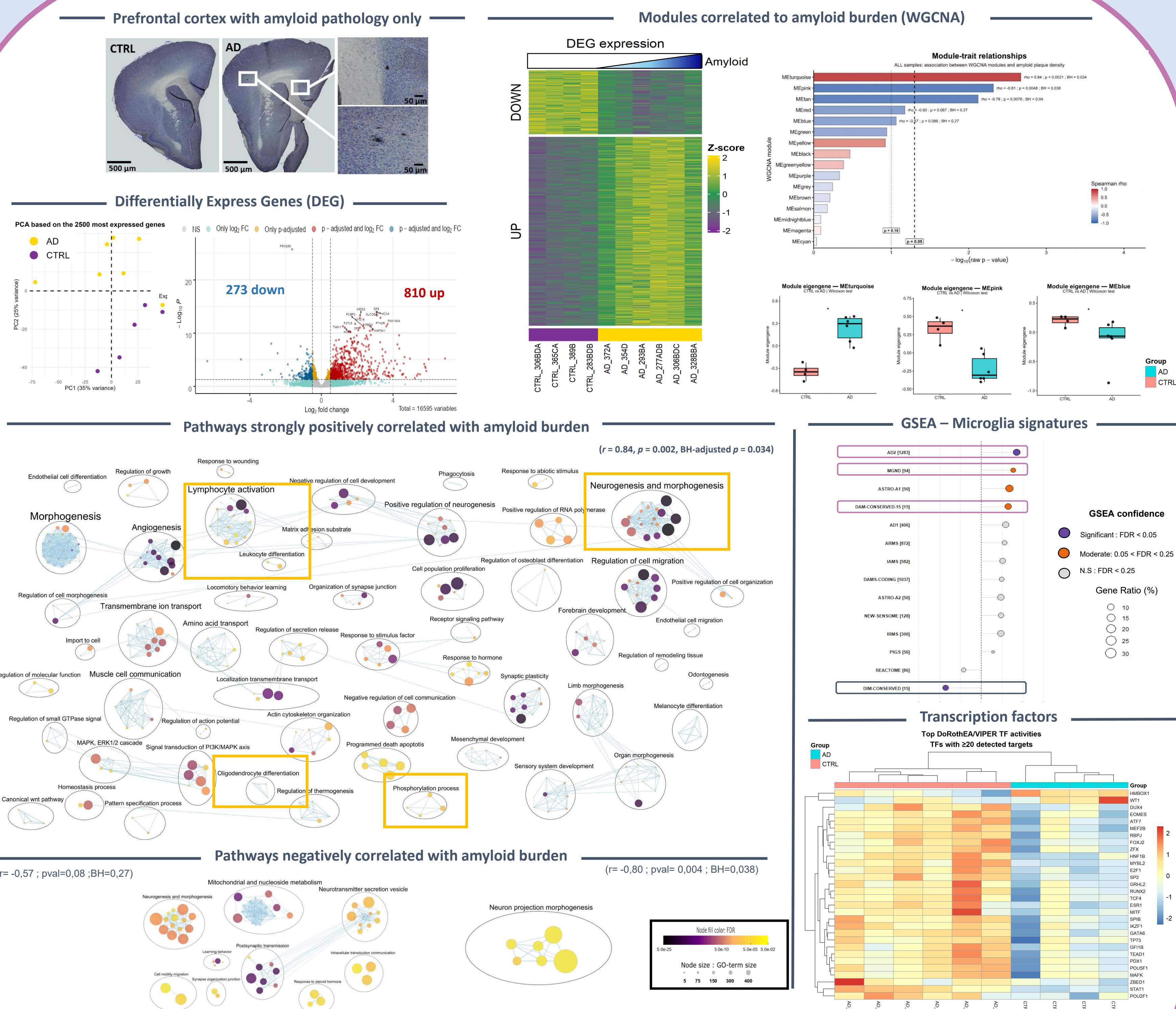


Primate model of amyloidosis, tauopathy and cognitive impairment



Aims: Identify the impact of intracerebral inoculation of human AD brain homogenates on the primate transcriptome

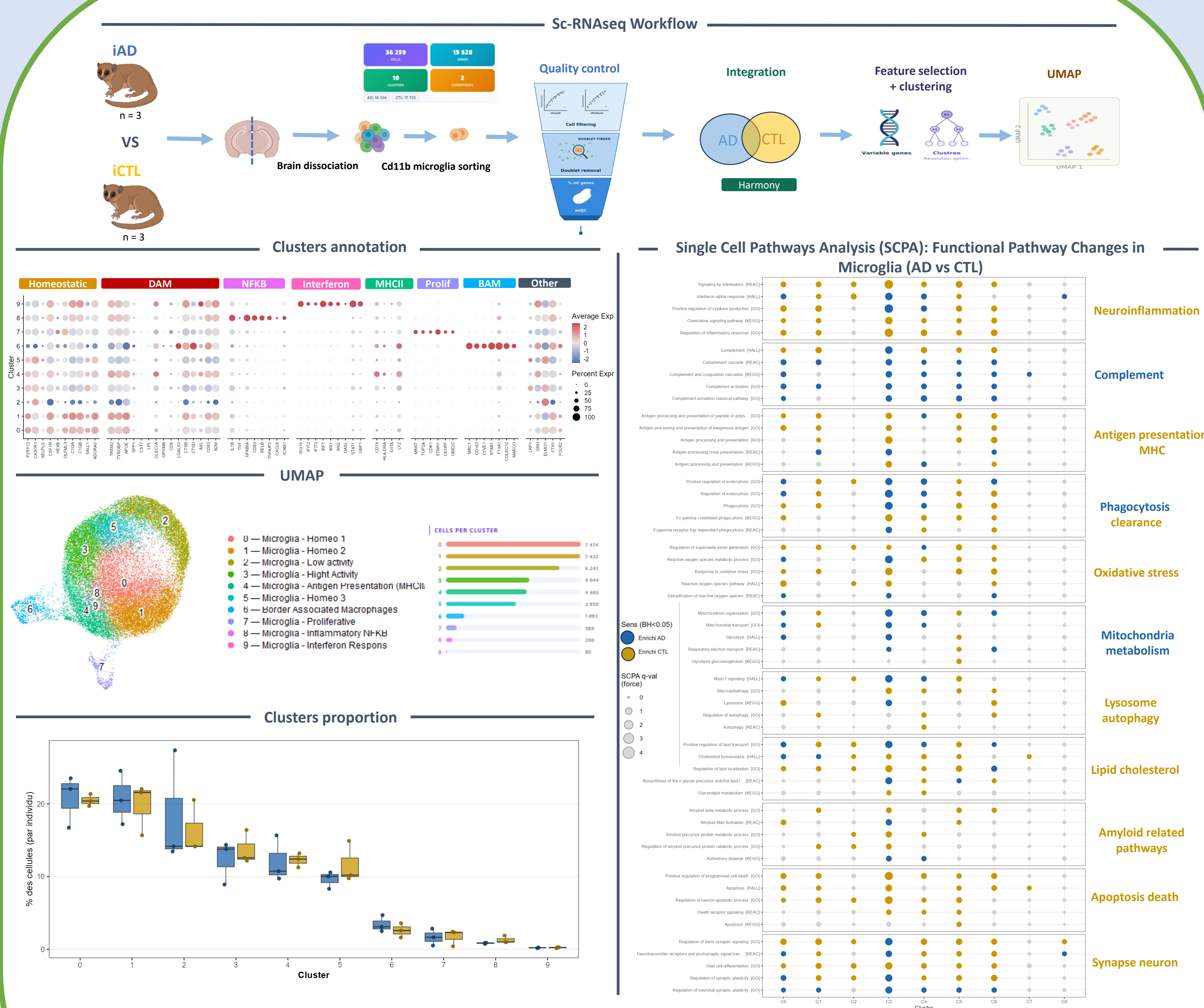
Amyloid impact on transcriptome in AD: RNAseq study



Ab burden in our AD-induced primate model is correlated to:

- An increase in adaptive immune activation, neurogenesis, and phosphorylation pathways
- Altered mitochondrial metabolism
- Slight microglial activation and a shift in Transcription factors

Effect of AD induction on microglial transcriptome



Microglial transcriptomic changes induced by AD injection in our primate model:

- No changes in microglial cluster proportion
- Overall, it seems that AD microglia are less activated than in CTL except for Complement, Phagocytosis and Mitochondrial Metabolism

Future directions:

Intercluster communication: CellChat NicheNet
How does AD induction impact astrocyte transcriptome? And glial cells crosstalk?

References:

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