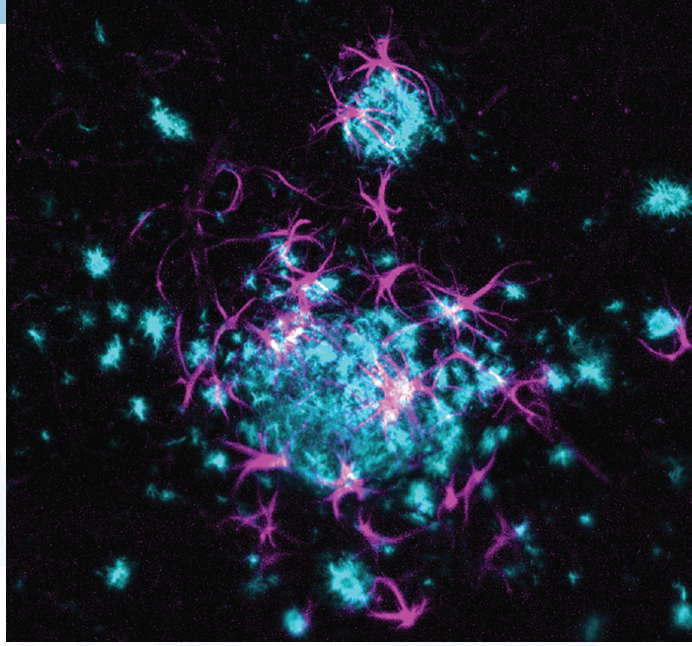
Alzheimer's Disease Models

Amyloid beta (Aβ) plaques and neurofibrillary tangles (NFTs), along with cognitive decline, are defining hallmarks of Alzheimer's disease. Understanding how these pathological features develop and discovering effective therapeutics to stop them is essential in the fight against this devastating condition. Taconic Biosciences offers a robust portfolio of transgenic rodent models that reliably develop both plaques and tangles. These models are invaluable tools for deepening our knowledge of Alzheimer's disease mechanisms and accelerating the development of novel therapies for Alzheimer's and other neurodegenerative disorders.



Clustering of microglia and astrocytes are in the proximity of the beta-amyloid plaque deposits.

FAMILIAL ALZHEIMER'S DISEASE MODELS

Tau/JNPL3 (Tau P301L mutation; Model 2508)
APPSWE (APP Swedish mutation; Model 1349)
APPSWE Tau (APP Swedish + Tau P301L; Model 2469)
ARTE10/APP PS1 (APP Swedish + PSEN1 M146V; Model 16347)

SPORADIC ALZHEIMER'S DISEASE MODELS

Humanized APOE2 Knock-in (Model 1547)
Humanized APOE3 Knock-in (Model 1548)
Humanized APOE4 Knock-in (Model 1549)

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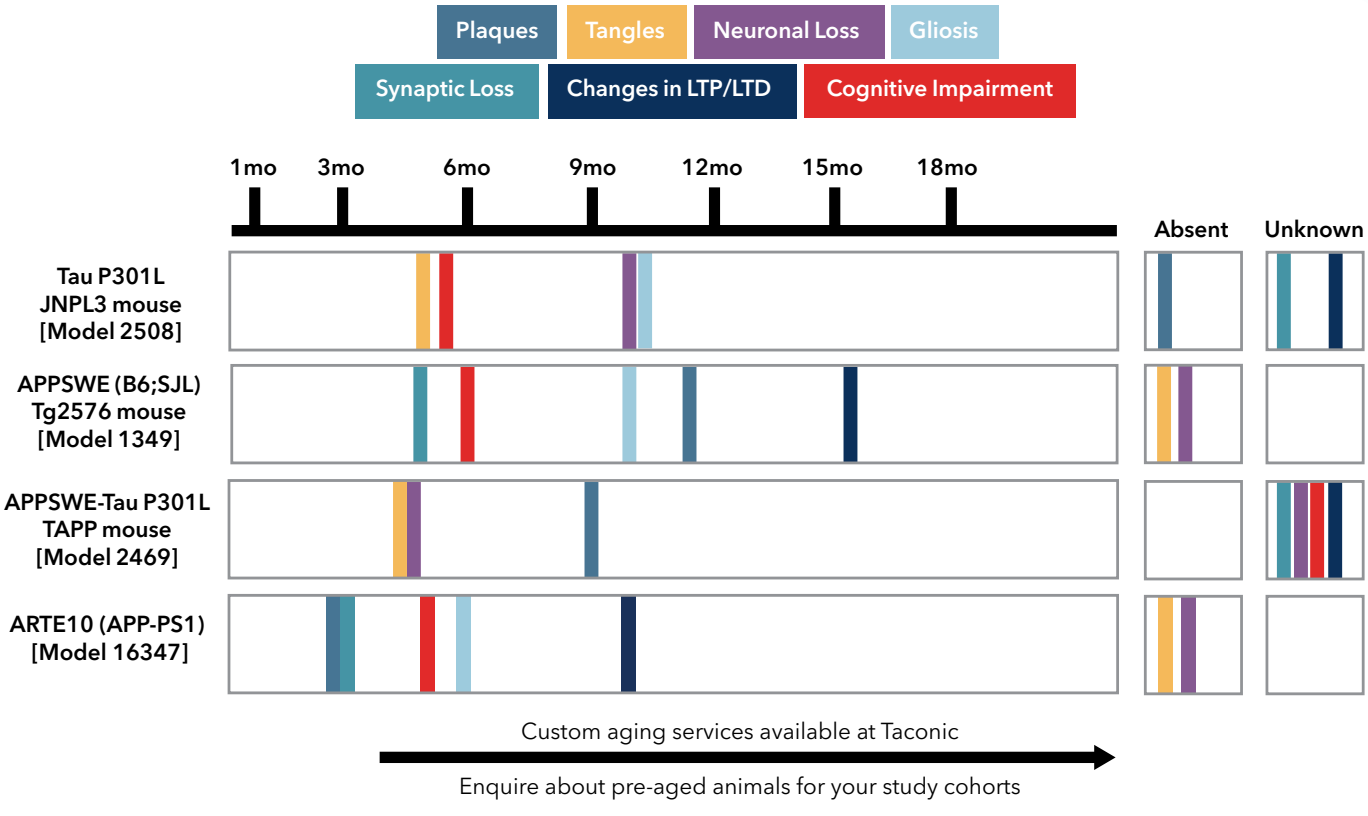
TIMELINE OF NEUROPATHOLOGY OF POPULAR ALZHEIMER'S MOUSE MODELS AVAILABLE FROM TACONIC

Graphic adapted from 'Research Models Visualization" at **www.alzforum.org**



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WHOLE-BRAIN 3D IMAGING OF CONGOPHILIC AMYLOID PLAQUES

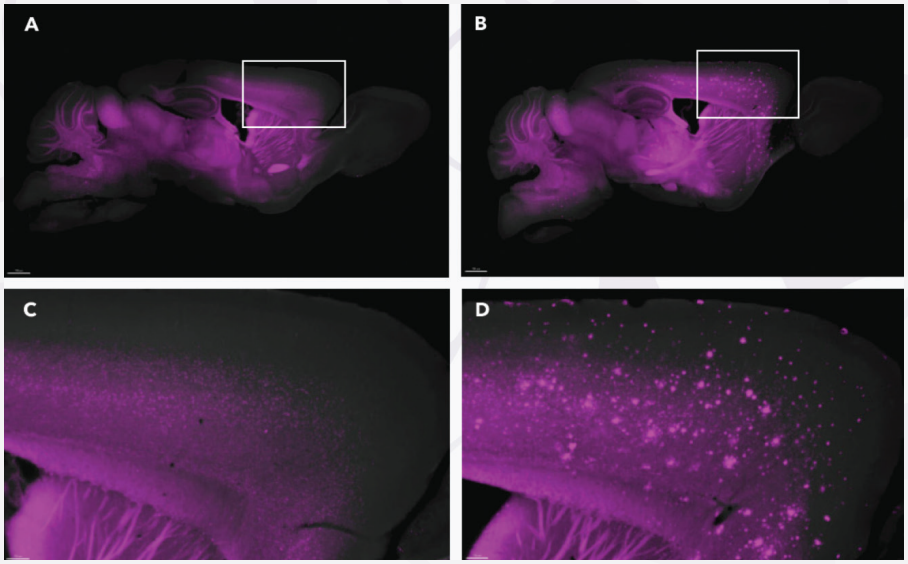
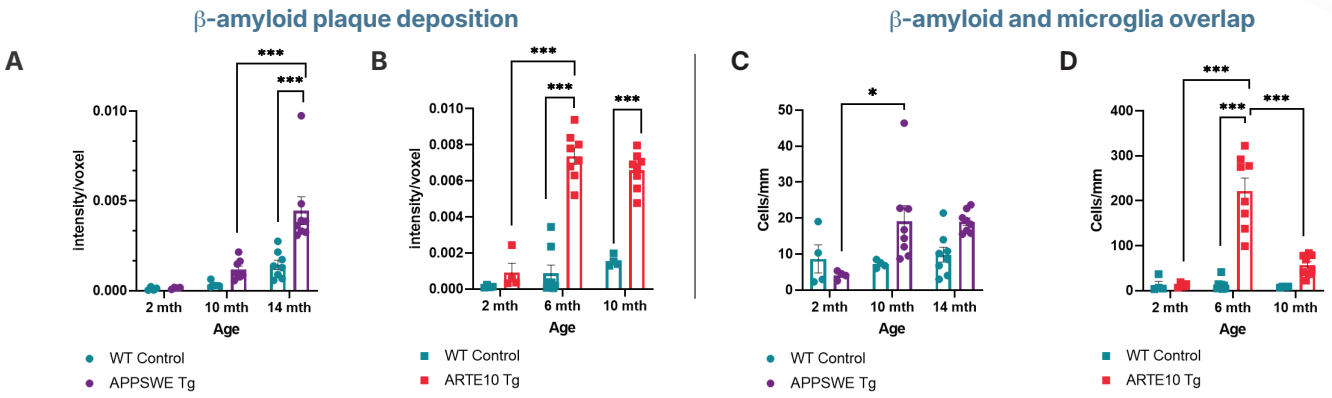


Figure 2. Whole-brain imaging of congophilic amyloid plaque deposition. **(A,B)** Parasagittal digital micrographs of Congo red-stained whole-brain of age-matched wild-type **(A)**, and A RTE10 **(B)** mouse. Scale bars = 700 µm. **(C,D)** Further magnification of boxed area in panels A and B. Scale bar, 150 µm.

β-AMYLOID PLAQUE DEPOSITION AND MICROGLIA OVERLAP IN HIPPOCAMPUS



β-Amyloid Plaque Deposition and Microglia Co-localization in APPSWE and ARTE10 mice. Intensity of plaques per voxel **(A and B)** and density of microglia cells on plaques **(C and D)** calculated for entire hippocampus per animal (n=4-8 per group) for the APPSWE model **(A and C)** and ARTE10 model **(B and D)**. Plaque deposition was significantly increased relative to wild type **(WT)** controls by 6 months of age for ARTE10 mice **(B)**, whereas plaques were not significantly increased in the APPSWE mice until 14 months of age **(A)**. Microglia overlap with plaques differently in the APPSWE and ARTE10 models, following a U shape function in the ARTE10 mice specifically **(D)**. Similar findings were found in the cerebral cortex.

Behavioral Phenotype Summary for the ARTE10 Mouse Model

ARTE10 Effect				
Indication	Test	5 months of age	10 months of age	Significance
Anxiety	Canopy Test	↑	↑↑	Increased anxiety-like behavior
Motivation/Mood	Nest Building	↓	↓	Decreased motivation/mood (increased latency to nest and lower nest scores)
Sensory Motor Gating	PPI	↓	↓	Deficits in sensory motor gating (reduced pre-pulse inhibition)
Activity/Locomotion	LMA	↓	↓	Hypolocomotion
Motor Function	Rotarod	NS	NS	No motor impairments
Activity	Running Wheel	↑	↑	Hyperactive
Learning	MWM*	↓	↓	Spatial working memory deficit
Memory	MWM* Y-Maze	NS NS	↓ ↓	Impaired working memory by 10 months

***MWM:** Morris Water Maze, PPI: Pre-pulse inhibition, LMA: Locomotor Activity, NS: not significant.

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