inotiv
analyze. answer. advance.

Advanced Alzheimer's Disease Research

Optimized Experimental Disease Models and Assays

Inotiv offers disease models and assays that are optimized to deliver translationally relevant data to guide your Alzheimer's disease (AD) research programs. Powered by our legacy companies, such as Envigo, Bolder BioPATH, and Histotox Labs, our models and services will propel the early discovery and nonclinical development of your AD therapies.

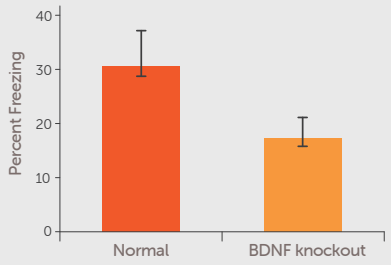
Genetically Engineered Rat Models

Inotiv is your only source for genetically engineered rat models of AD. Originally created at SAGE Labs, Inc., these models were developed using advanced technology to replicate aspects of AD phenotypes.

- ApoE knockout rat
- App knockout rat
- BDNF knockout rat
- Humanized ApoE2 knockin rat
- Humanized ApoE3 knockin rat
- Humanized ApoE4 knockin rat

Figure 1 Freezing Behavior in BDNF Knockout Rats

BDNF knockout rats (orange bar) exhibit reduced freezing behavior compared to normal animals (red bar) during contextual fear conditioning, suggesting deficits in learning and memory.

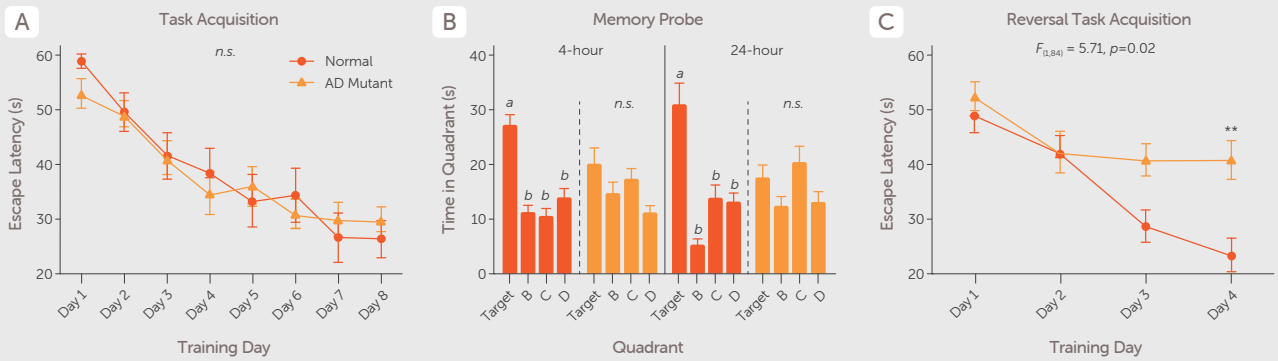


Behavioral Assays in Rats and Mice

Inotiv offers a comprehensive suite of behavioral assays. These assays have been validated in a transgenic mouse model of AD, as well as in a model delivering amyloid-β through intracranial injections. Additionally, we maintain the flexibility to validate these assays in your model of interest.

- Open field assay (OFA)
- Elevated plus maze (EPM)
- Morris water maze (MWM)
- Barnes maze
- Contextual fear conditioning (CFC)
- Gait analysis

Figure 2 Cognitive Deficits in a Mouse Model of AD



Mice carrying mutations related to AD have reduced cognitive function. **A)** Both AD mutants (orange line) and normal mice (red line) learned the initial location of the hidden platform. **B)** The mutants (orange bars), though, did not remember the target quadrant 4 and 24 hours after the last training trial, while normal mice did (red bars). **C)** During reversal learning, normal mice were trained to the new quadrant (red line), but AD mutants failed (orange line). Data sets that do not share any letters differed significantly. (*n.s.*= not significant).

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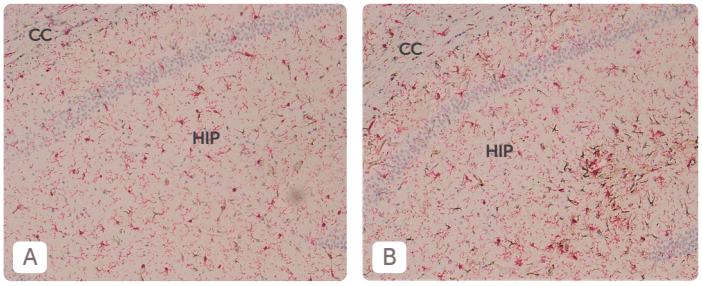
Histopathological Assessment

Inotiv offers a full range of immunohistochemistry, histopathology, and image analysis/digital pathology services. Utilize our expert scientists to evaluate neural tissue from your animal model for pathological features of AD, including:

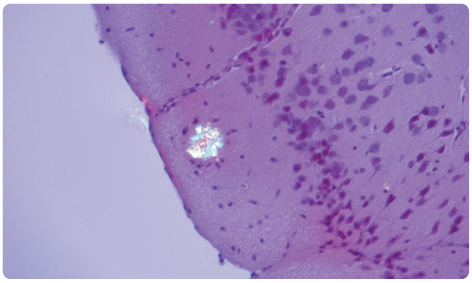
- Plaque formation
- Astrogliosis
- Microglial activation
- Synaptic loss
- Neuronal loss

Figure 3 Pronounced Astrogliosis in a Mouse Model of AD



Glial cells were detected in perfusion fixed, paraffin embedded brains from 12-month-old wild type **(A)** and AD **(B)** mice. Gliosis was evaluated by detecting reactive astrocytes and microglia via expression of GFAP (brown) and Iba1 (red), respectively. The tissue was stained with H&E. CC = corpus callosum. HIP = hippocampus.

Figure 4 Amyloid Plaques in a Mouse Model of AD



Amyloid plaques were visualized in perfusion fixed, paraffin embedded brains from 12-month-old AD mice by staining with Congo red and illuminating with polarized light.

Additional Services for AD Research

Inotiv's capabilities extend beyond models and behavioral testing and includes additional GLP and non-GLP *in vivo* and *in vitro* services and assays that can be customized to provide solutions for your AD research program.

- Stereotaxic surgery
- Tissue harvesting
- Oxidative stress enzymology
- Cytokine analysis with ELISA and Luminex® Assays
- CBC/clinical chemistry analysis
- Mass spectrometry proteomics
- Primary neural cell culturing
- Human stem cell and brain organoid culturing
- Confocal & electron microscopy

Contact us at inotivco.com/contact to discuss how our models and services can support your AD research.