

Bolder BioPATH, Inc.

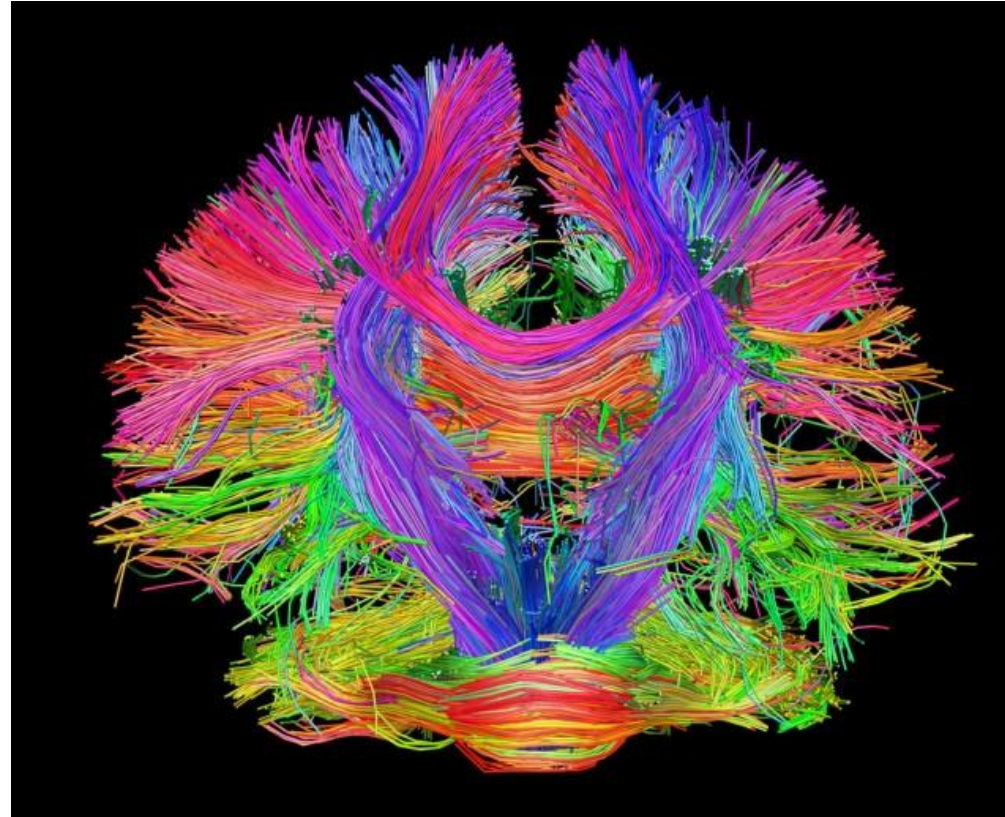
Boulder, Colorado. Est. 2003



Pre-Clinical Contract Research Organization



50% of the Top 10 Health Concerns are directly related to brain function



Key growth areas of sports physiology, weight management, mental health, sleep, mood, menopause, sexual health, vision and aging all touch on the brain health space



CNS/Neuroscience

What do your ideas look like in the market?

Support current & new products by filling known gaps in their brain health data

Determine how genetics and epigenetics affect therapeutic needs

Interactions with lung, cardiovascular and gut health

What are your activities? How do we best support your needs?

Customers

Academia

Regulatory

Key Opinion Leaders (KOLs)

CNS/NEUROSCIENCE

PROOF-OF-CONCEPT AND EFFICACY FOR YOUR CURRENT AND FUTURE PRODUCTS

- 1 Grow & Defend current & future portfolios by acquiring supportive data
- 2 Develop & Support sophisticated collaborations for long-term capabilities
- 3 Improve the understanding of the interactions between treatments, genetics and environmental influences



✓ Pre-clinical expertise

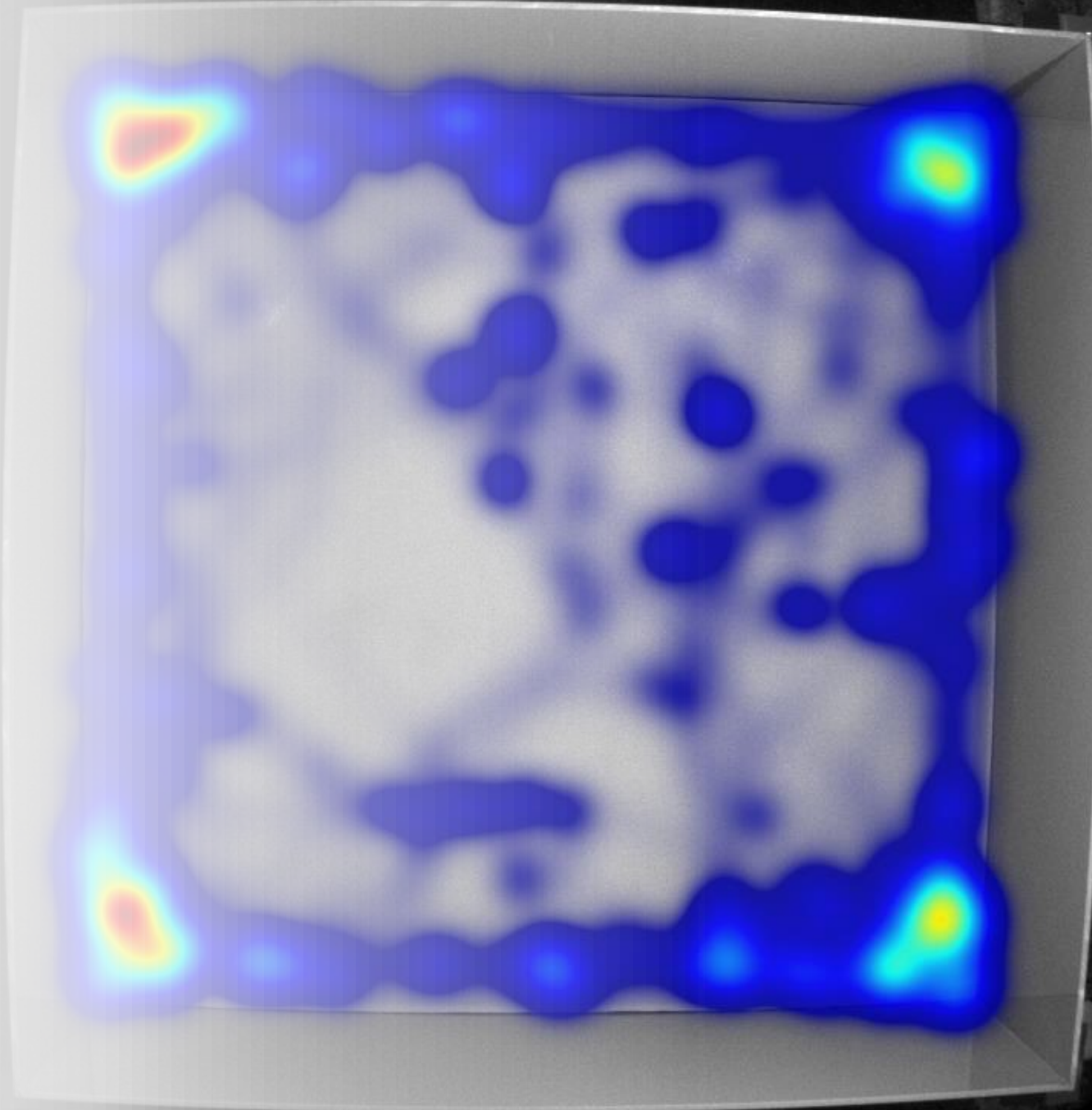
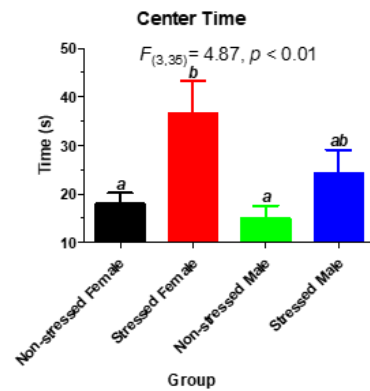
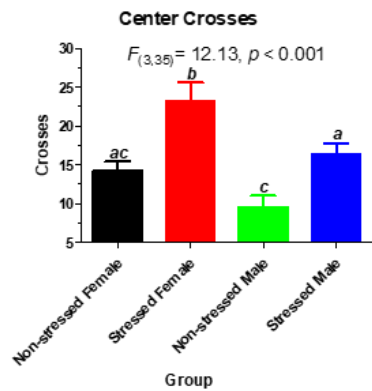
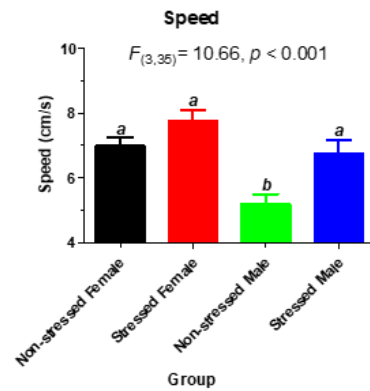
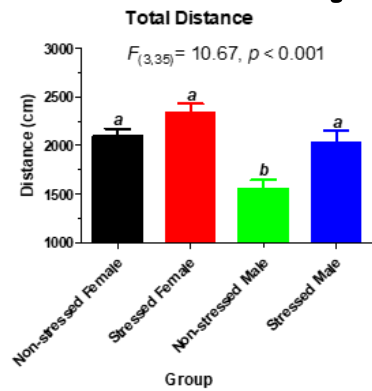
✓ Active Research Partnerships



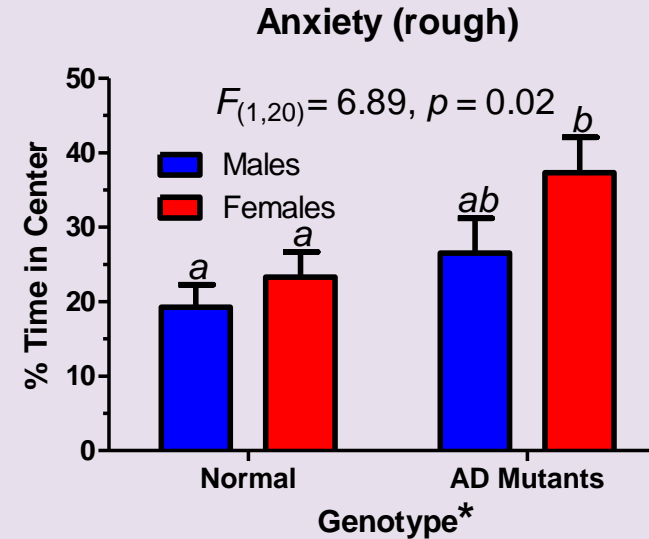
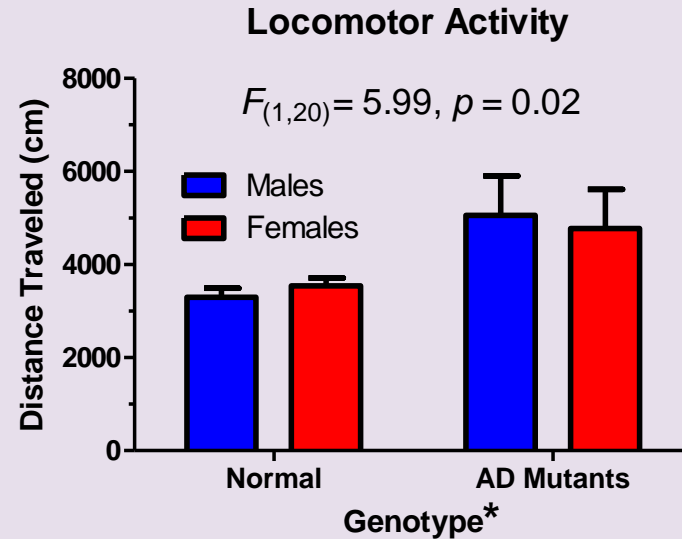
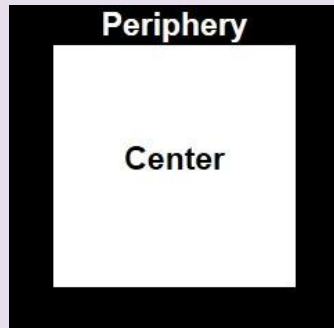
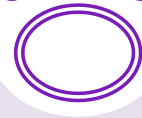
Open field for locomotor and anxiety



Open field for locomotor and anxiety



Alzheimer's mice (APP^{Swe}/Tg2576) exhibit altered dopamine neurochemistry at 6 months old



No effect of genotype in the elevated plus maze, a better measure of anxiety, suggesting that the above is a dopamine-related activity effect only; effects stronger in females

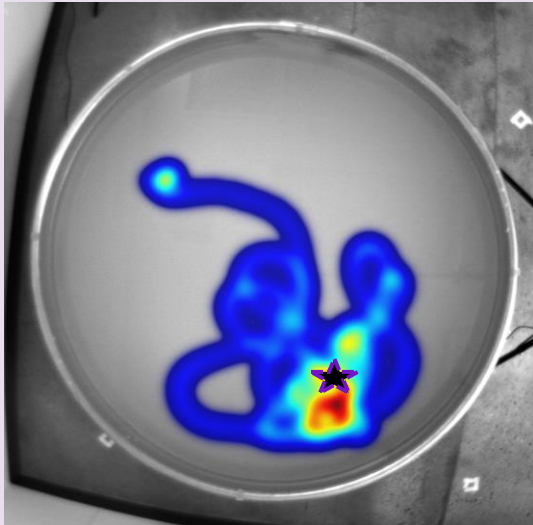


Morris water maze for cognition

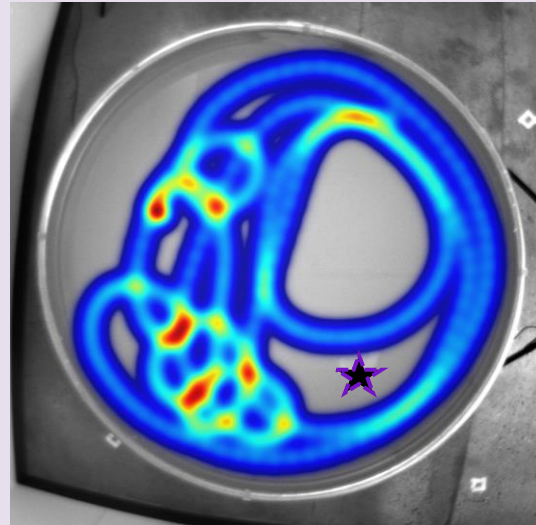


Male AD mutants have learning deficits, while female AD mutants show memory deficits at 7.5 mo

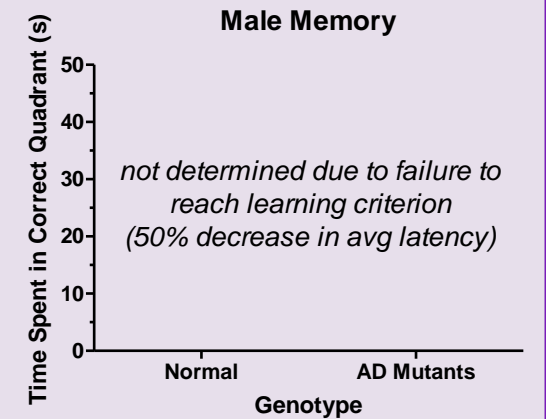
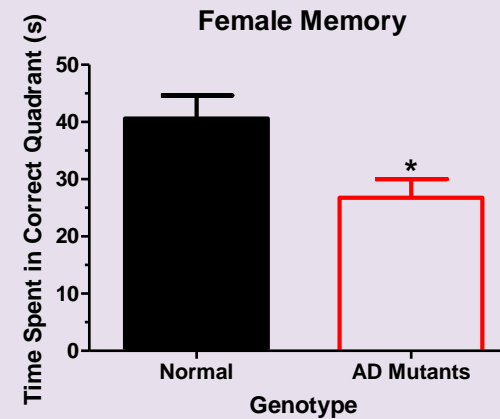
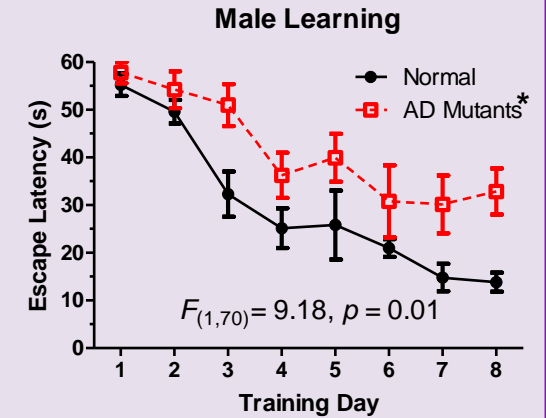
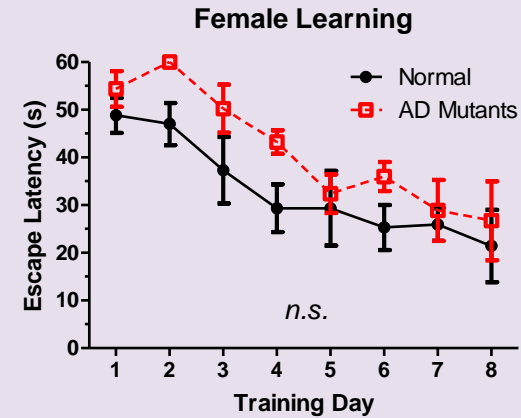
Wild-type mouse



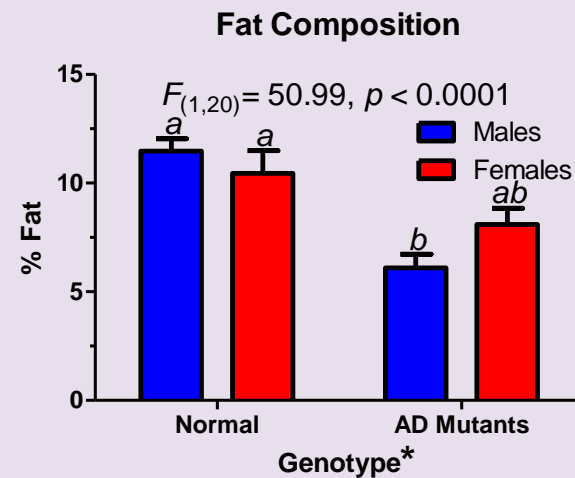
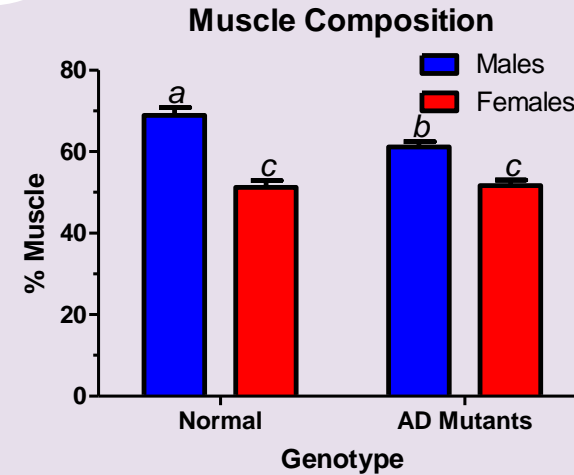
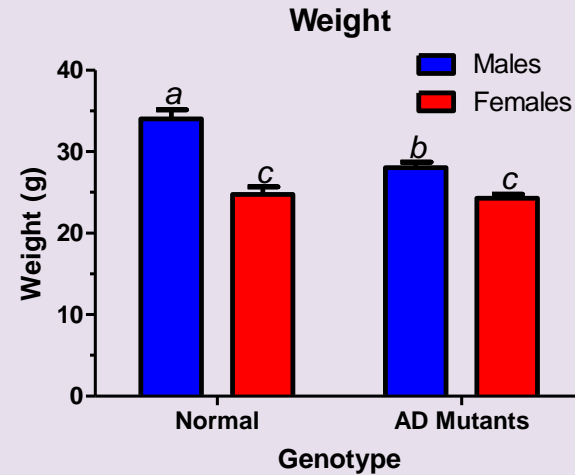
Alzheimer's disease mouse



MWM = Morris water maze; similar experiments in the Barnes maze were performed, but the AD mice did not explore



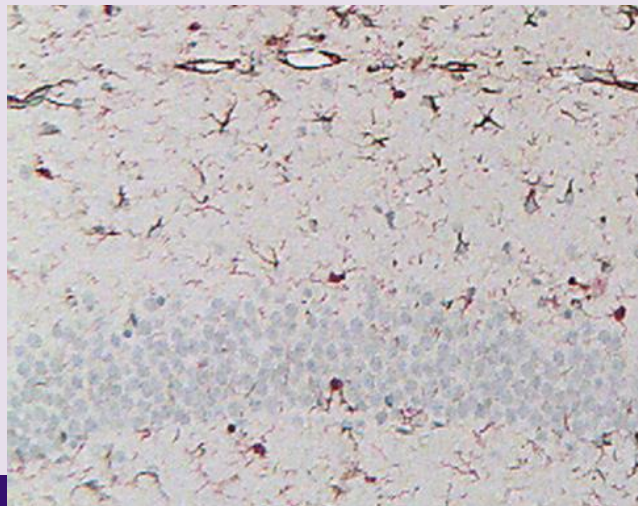
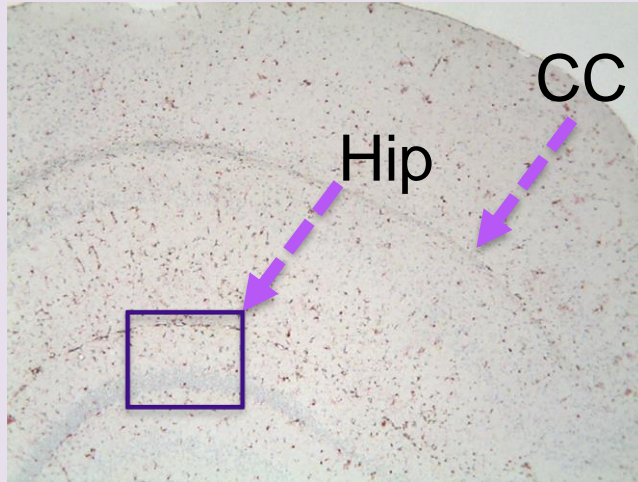
AD mice exhibit reduced fat at 8 months, but effects on weight & muscle are limited to males



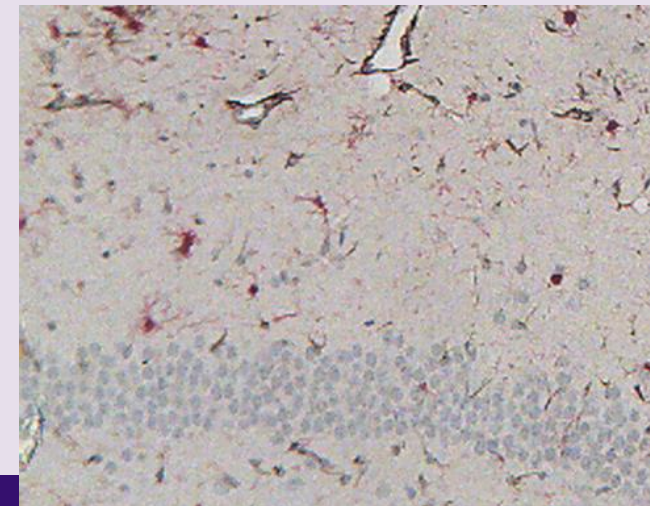
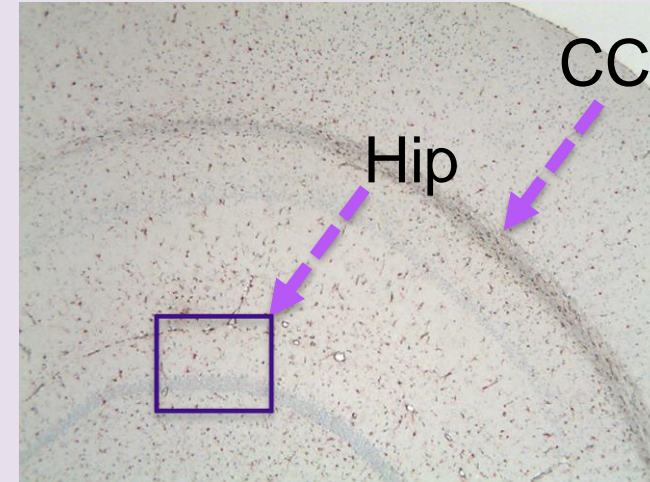
Beginnings of astrogliosis in the corpus callosum and hippocampus of AD mutants at 8 months



Normal



AD Mutant



Brown = Astrocytes (GFAP)
Red = Microglia (Iba1)
H&E background stain
CC = corpus callosum
Hip = hippocampus

Histology at 12 months (data expected by December 2020)



- Amyloid- β (Congo Red)
- Glial marker staining (GFAP & Iba1)
- All expected to be more pronounced than at 8 months

SKILL SET SUMMARY

- ***In vivo* capabilities in rats and mice (piglets and sheep available via 3rd-party collaboration)**
 - Surgery (e.g. OVX, ADX, s.c. & i.c. implants, stereotactic, i.v. catheterization, bone defect)
 - Video analysis of gait, exercise and male sexual performance
 - Monitoring of skin & body temperature (model of menopausal hot flash)
 - Open field (locomotor activity and anxiety)
 - Motor coordination (rotarod, etc.)
 - Elevated plus maze (anxiety-like), Forced swim test (depressive-like)
 - Morris Water Maze, Barnes Maze and fear conditioning(cognition)
 - Sociability
 - Sensory gating
 - Tissue harvesting for endpoint of choice
 - Fertility, EEG, Sleep, and Acute & Chronic inflammation in multiple systems available through in-house and 3rd-party collaborations
- ***In vitro* capabilities**
 - Human stem cells and brain organoids derived from them
 - Primary neurons, oligodendrocytes, astrocytes and microglia
 - Osteoblasts, retinal epithelial cells, cell lines and macrophages
- **Commonly used endpoints**
 - *In silico* and proteomic approaches to idea development & hypothesis generation
 - Multiplexed ELISA, immunohistochemistry, enzymology, electrophysiology
 - Confocal & electron microscopy (TEM and SEM)
 - Glutamate challenge, hypoxia challenge, oxidative stress, LPS stimulation
 - Biomarkers for viability, proliferation, growth, development/maturation and immune activation
- **Under development**
 - Integration with genetics and personalized medicine
 - Coordination and integration with other BBP models

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