



COLORADO STATE
UNIVERSITY

Integrating Translational Models to Study Neurodegeneration in Geriatric Dogs with Cognitive Dysfunction

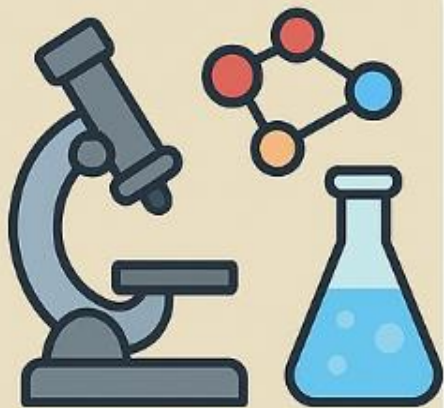
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Associate Professor

Environmental and Radiological Health
Sciences

‘Doggy Dementia’ Canine Cognitive Dysfunction Syndrome





BENCHWORK



**PRECLINICAL
ANIMAL
MODELS**

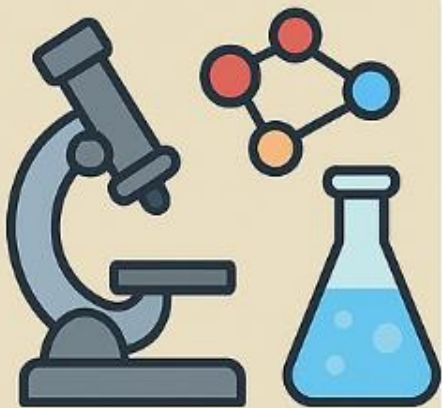


**TRANSLATIONAL
VETERINARY
TRIALS**



**HUMAN
CLINICAL
TRIALS**





BENCHWORK



**PRECLINICAL
ANIMAL
MODELS**



**TRANSLATIONAL
VETERINARY
TRIALS**



**HUMAN
CLINICAL
TRIALS**

Human

Dog

Healthy

Impaired

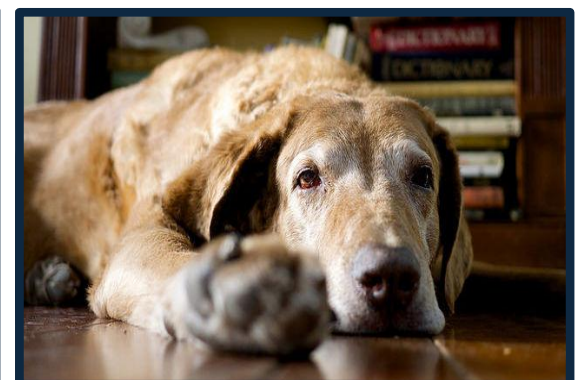
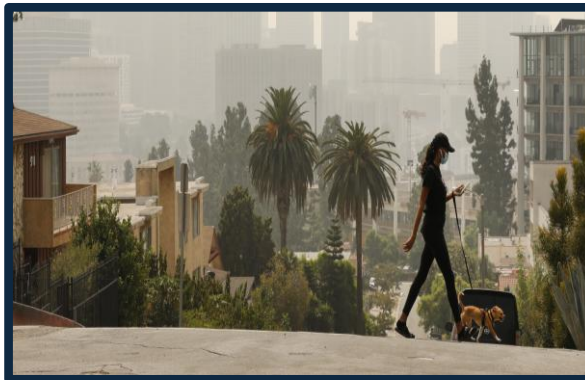
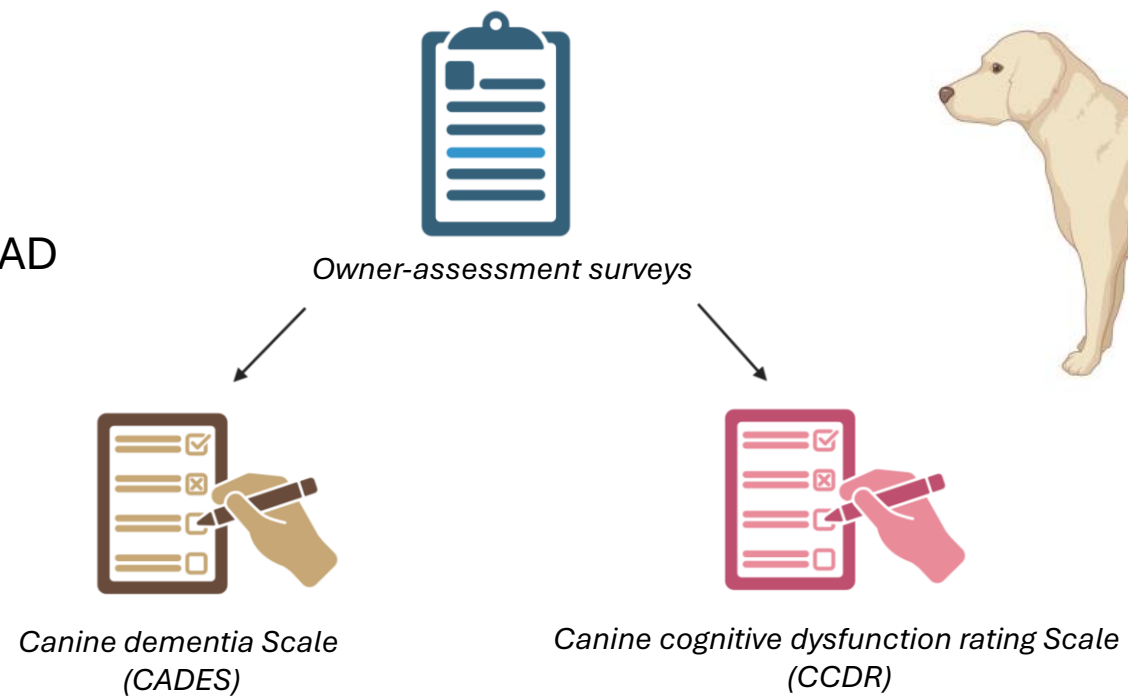


Are there better ways to determine if a therapy would translate to a human?

Can we study the aging brain better?

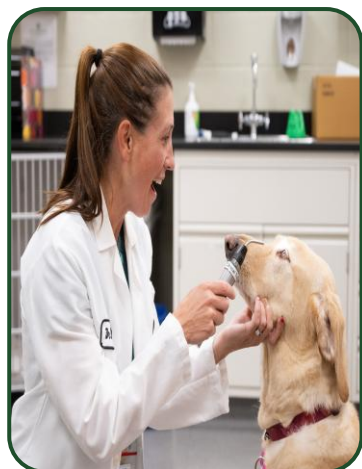
Canine Cognitive Dysfunction (CCD) in Companion Animals

- Similar pathology to AD
- Cognitive & behavioral changes related to AD
- Canines as a model for AD

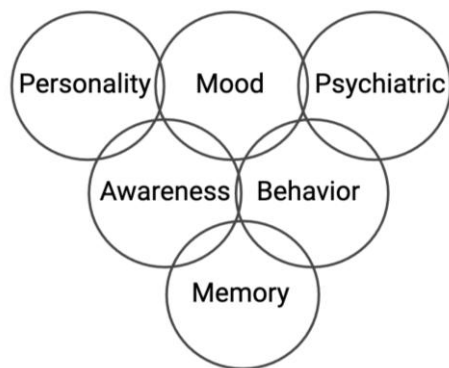


Evaluation of Canine Cognitive Dysfunction Syndrome (CCDS)

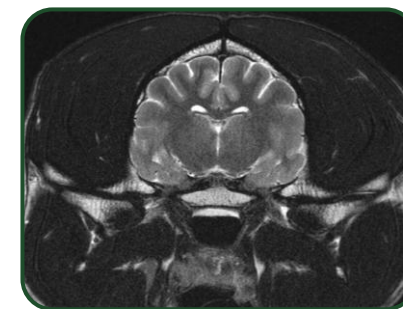
Clinical features



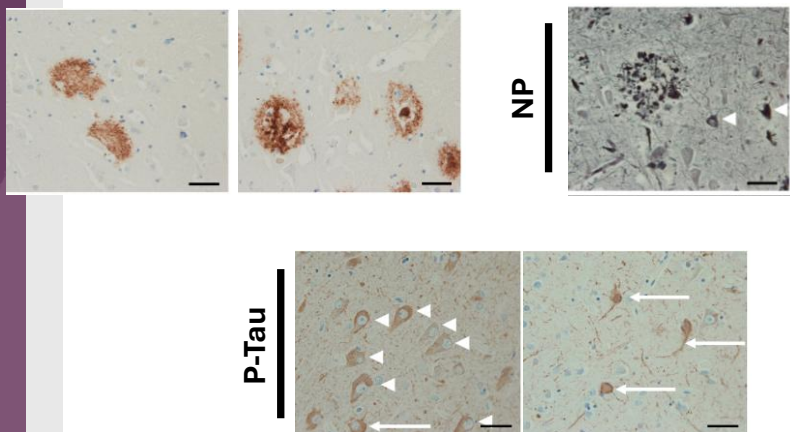
Behavioral features



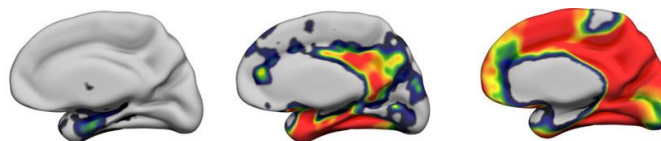
Imaging



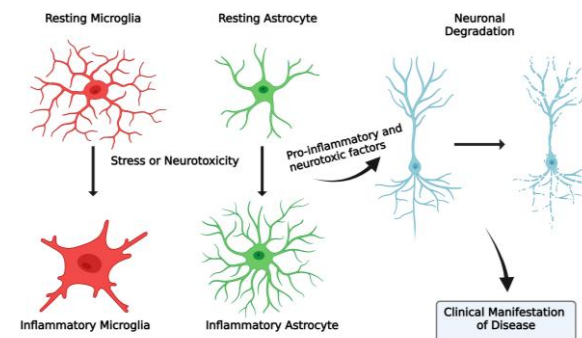
Microscopic features



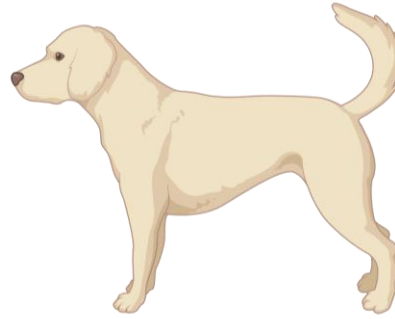
Neuropathological evaluation



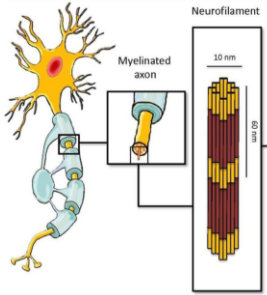
Cellular Stress signals



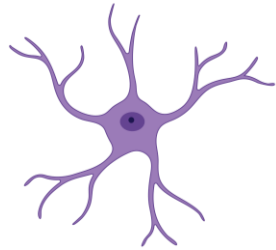
Approach



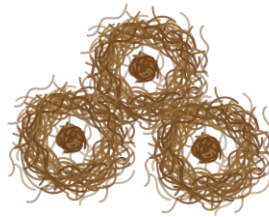
1 Bio-fluid analyses



Neurofilament light chain (NfL)

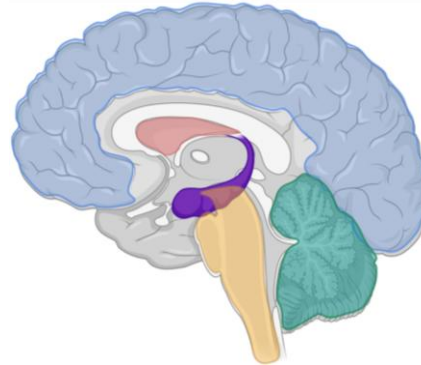


Glial fibrillary acidic protein (GFAP)

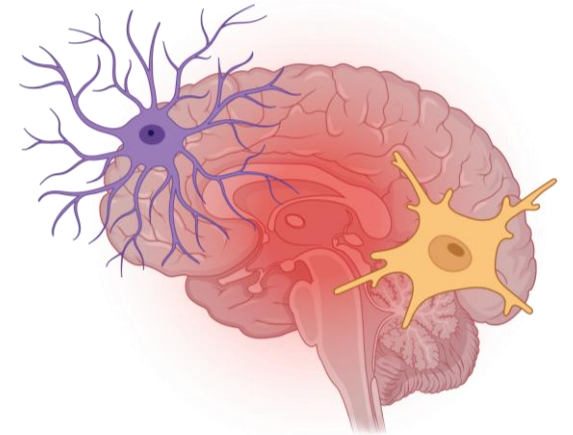


Beta-amyloid ($A\beta$)

2 Neuropathology

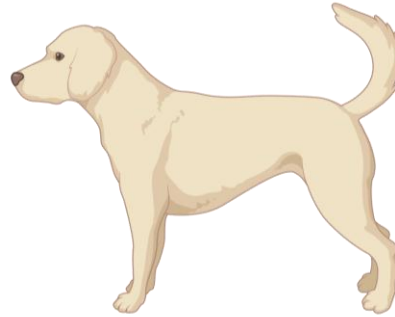


3 Neuroinflammation

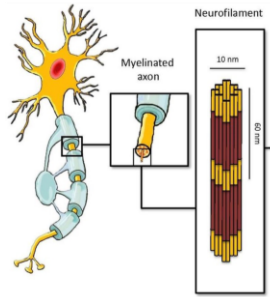


Elevated NfL and decrease in $A\beta_{1-42/1-40}$ ratio
Alsulami et al., 2025

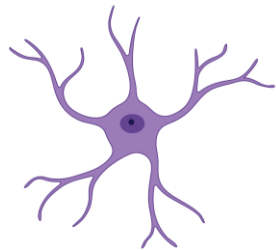
Approach



1 Bio-fluid analyses



Neurofilament light chain (NFL)

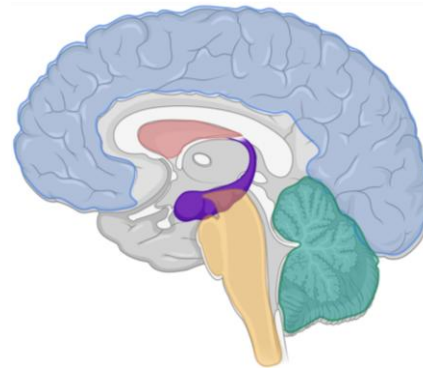


Glial fibrillary acidic protein (GFAP)

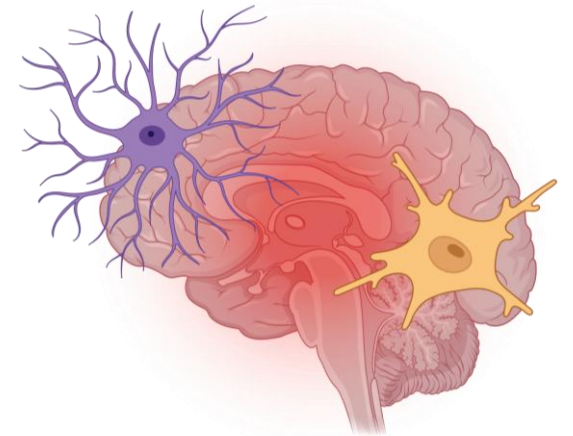


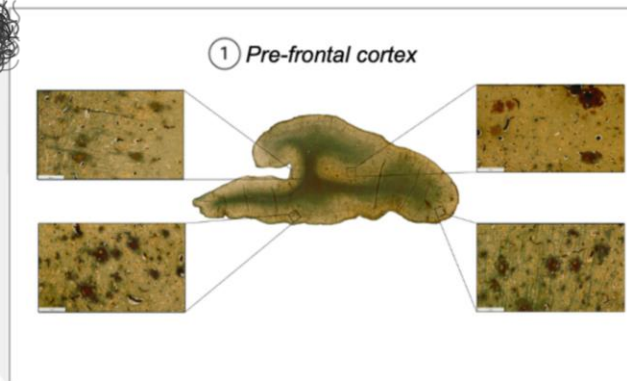
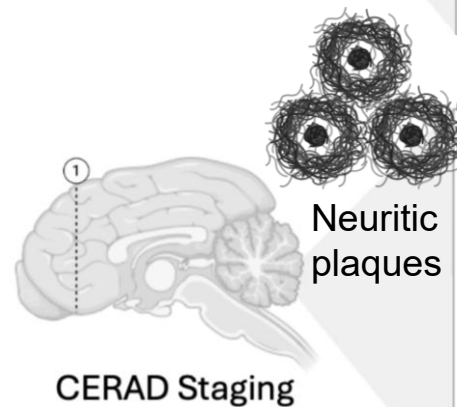
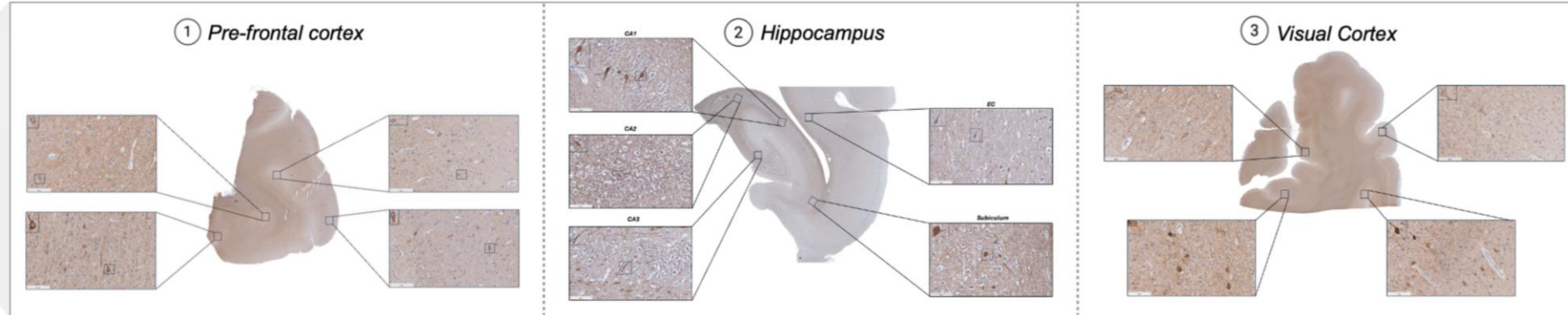
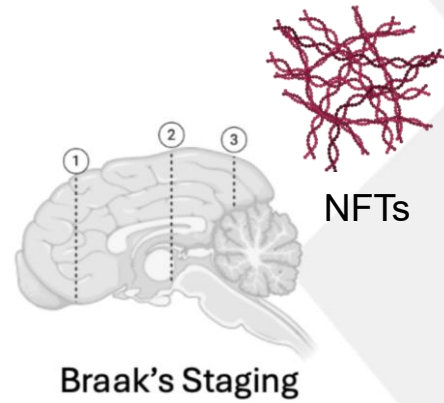
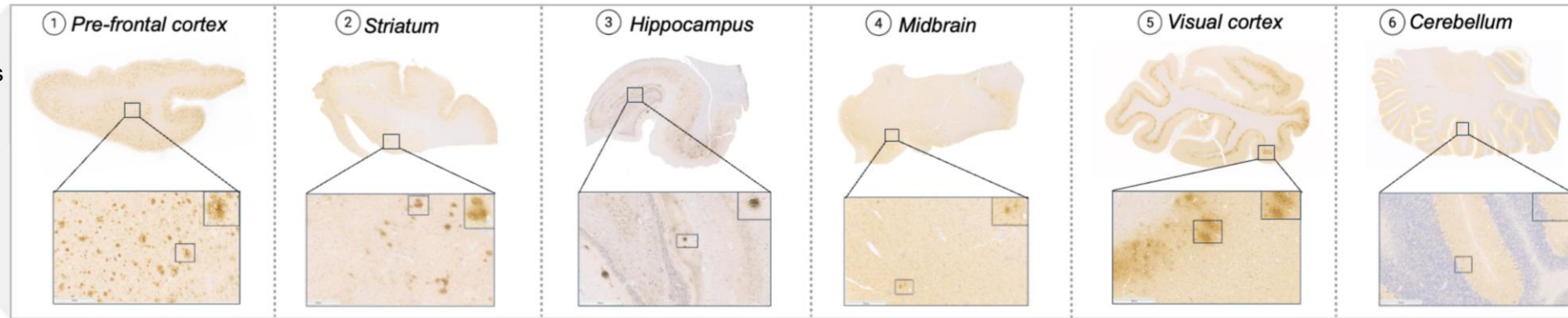
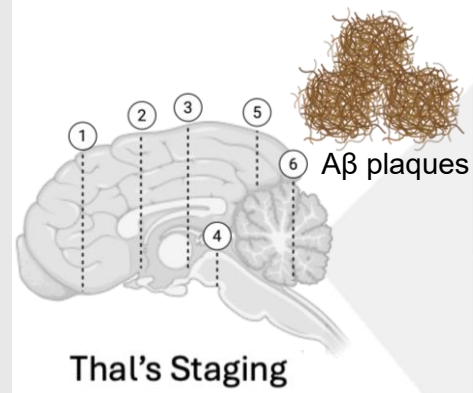
Beta-amyloid (Aβ)

2 Neuropathology



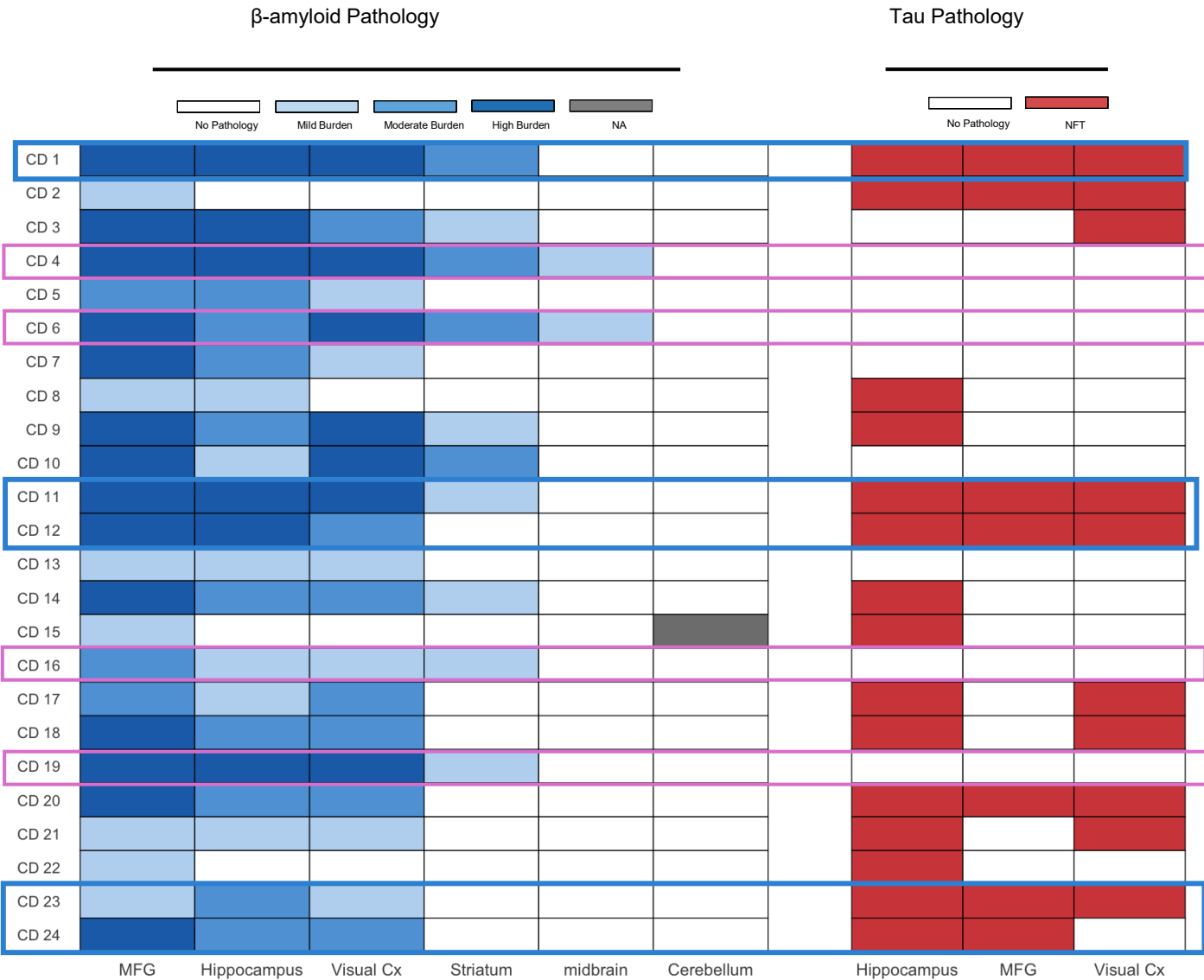
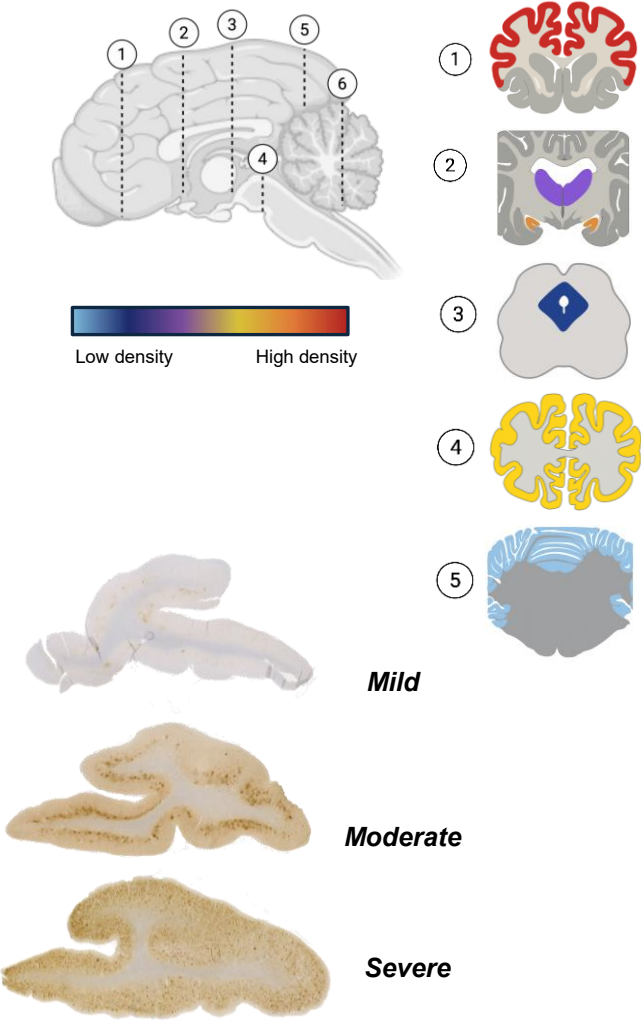
3 Neuroinflammation



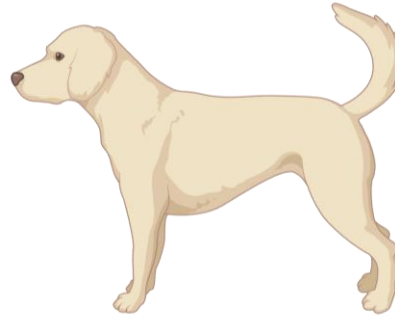


Human NIA-AA criteria were used as a translational framework to structure neuropathological evaluation in aging dogs

Semi-quantitative assessment “heterogeneity”



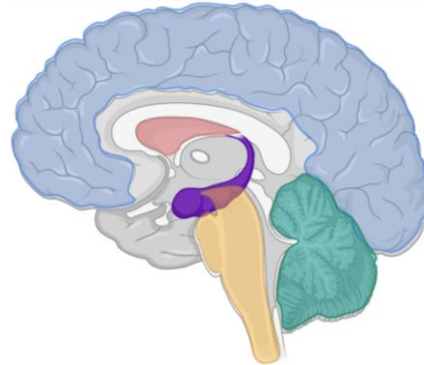
Approach



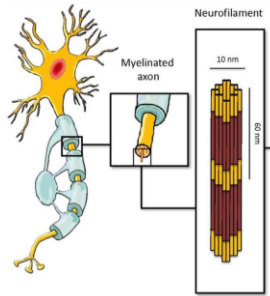
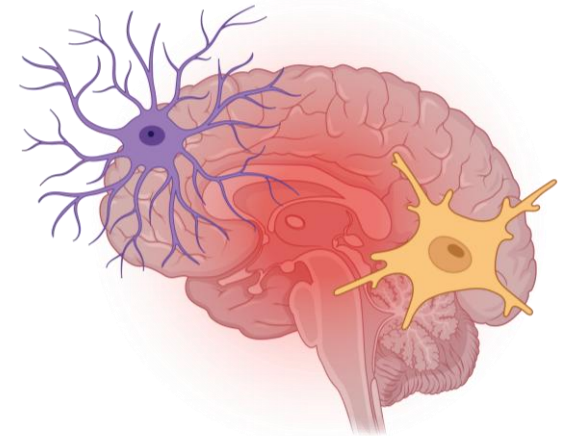
1 Bio-fluid analyses



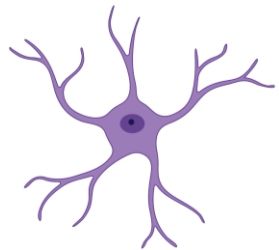
2 Neuropathology



3 Neuroinflammation



Neurofilament light chain (NFL)

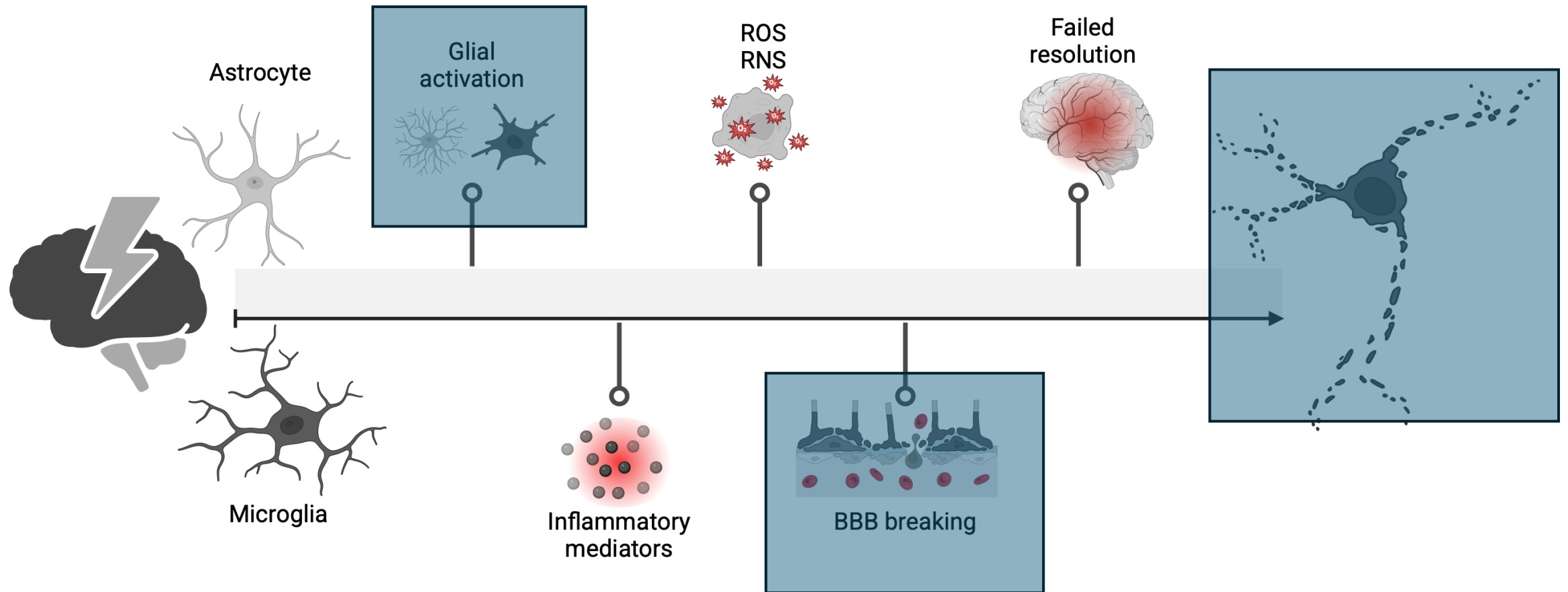


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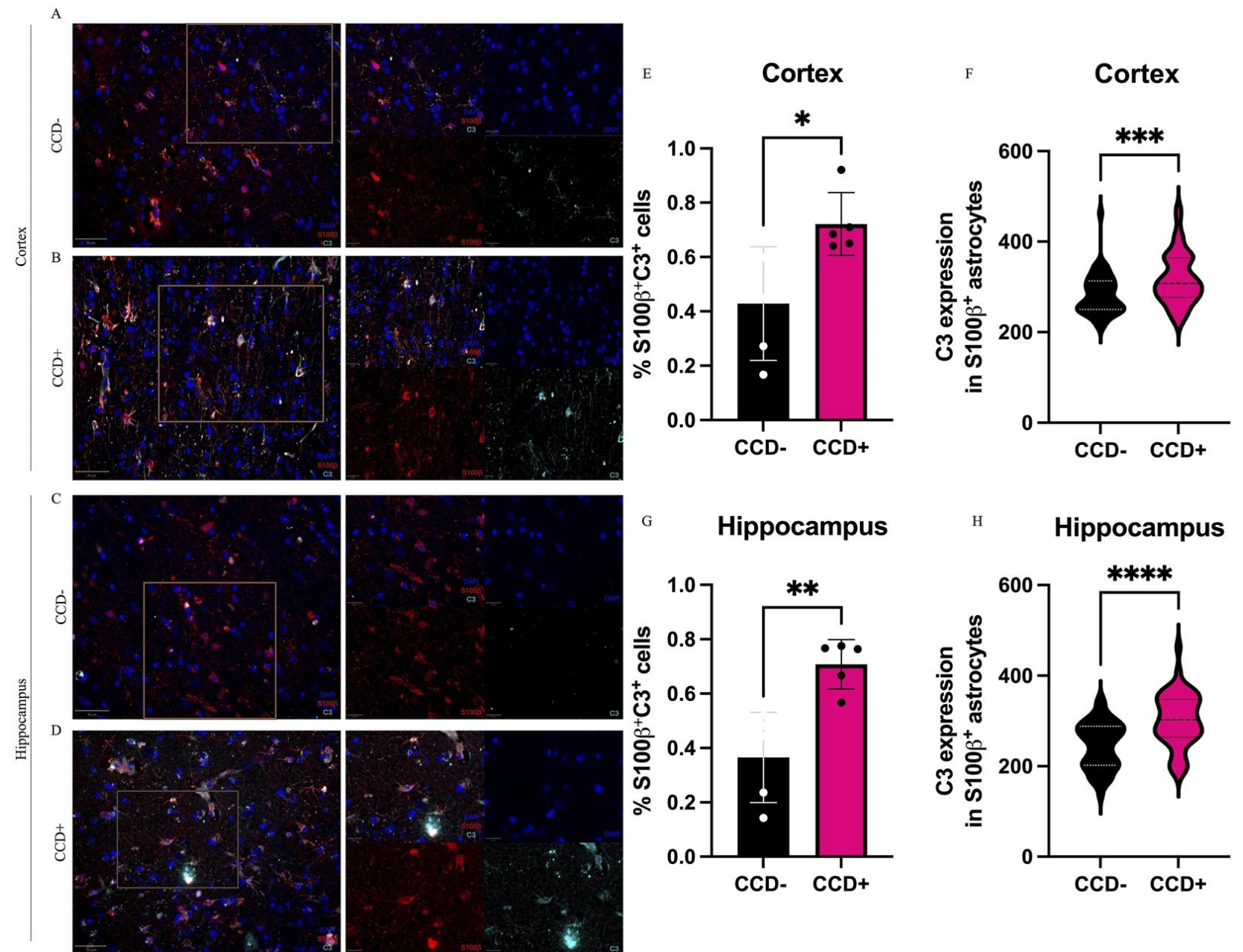


Beta-amyloid (A β)

Neuroinflammation and Neurotoxicity in the CCD+ brain

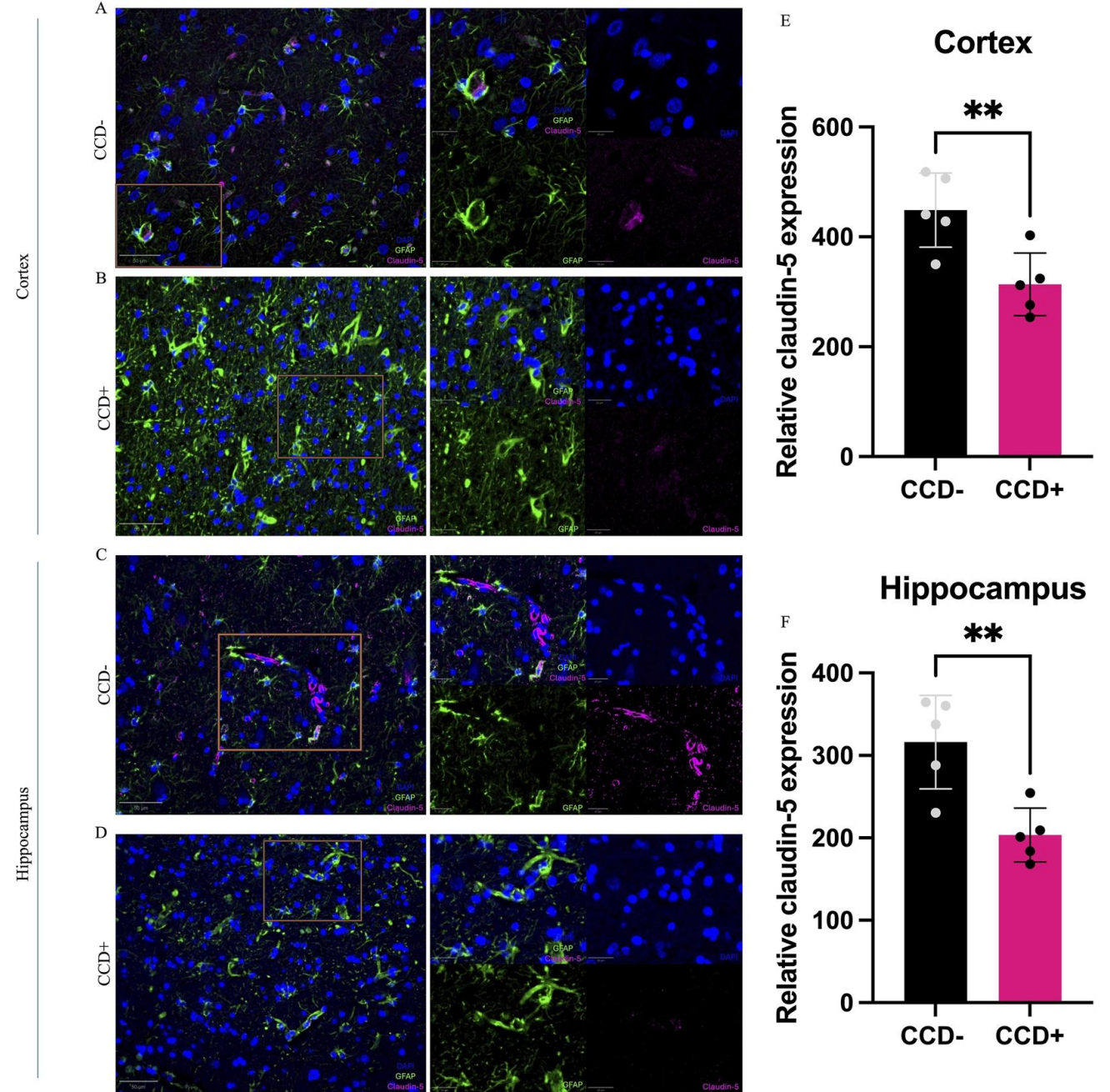


Neurotoxic
 $S100\beta^+C3^+$
astrocytes are
increased in the
cortex and
hippocampus of
CCD⁺ canines

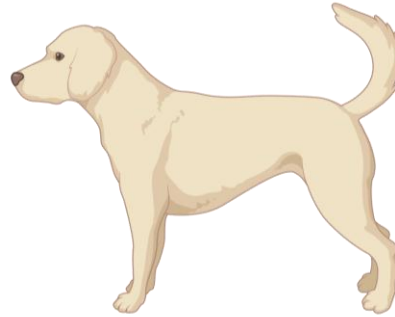


Claudin-5 expression is reduced in cortical and hippocampal microvessels of CCD⁺ canines

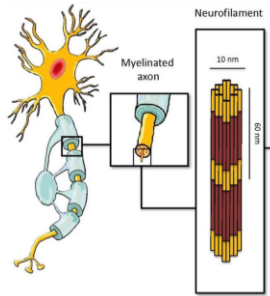
Boland et al., 2026



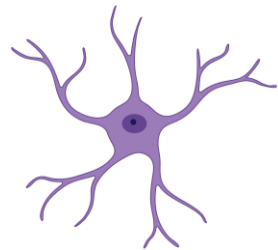
Approach



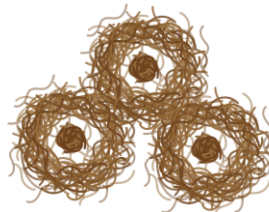
1 Bio-fluid analyses



Neurofilament light chain (NFL)

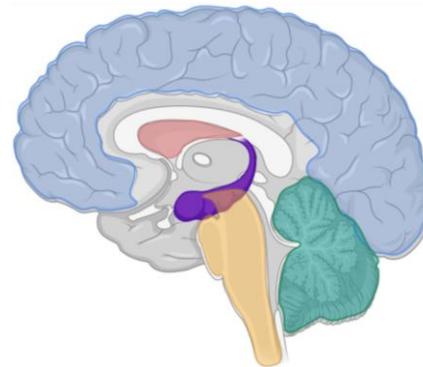


Glial fibrillary acidic protein (GFAP)

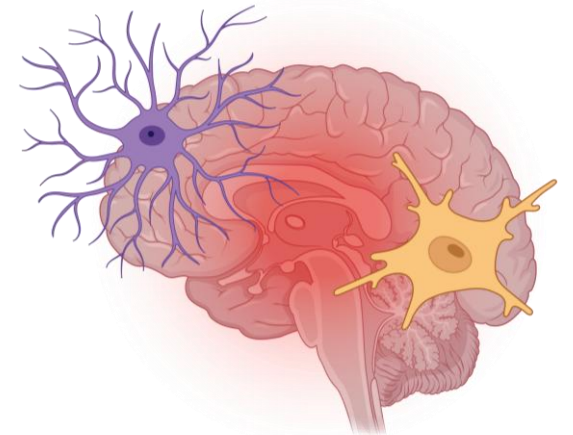


Beta-amyloid (Aβ)

2 Neuropathology

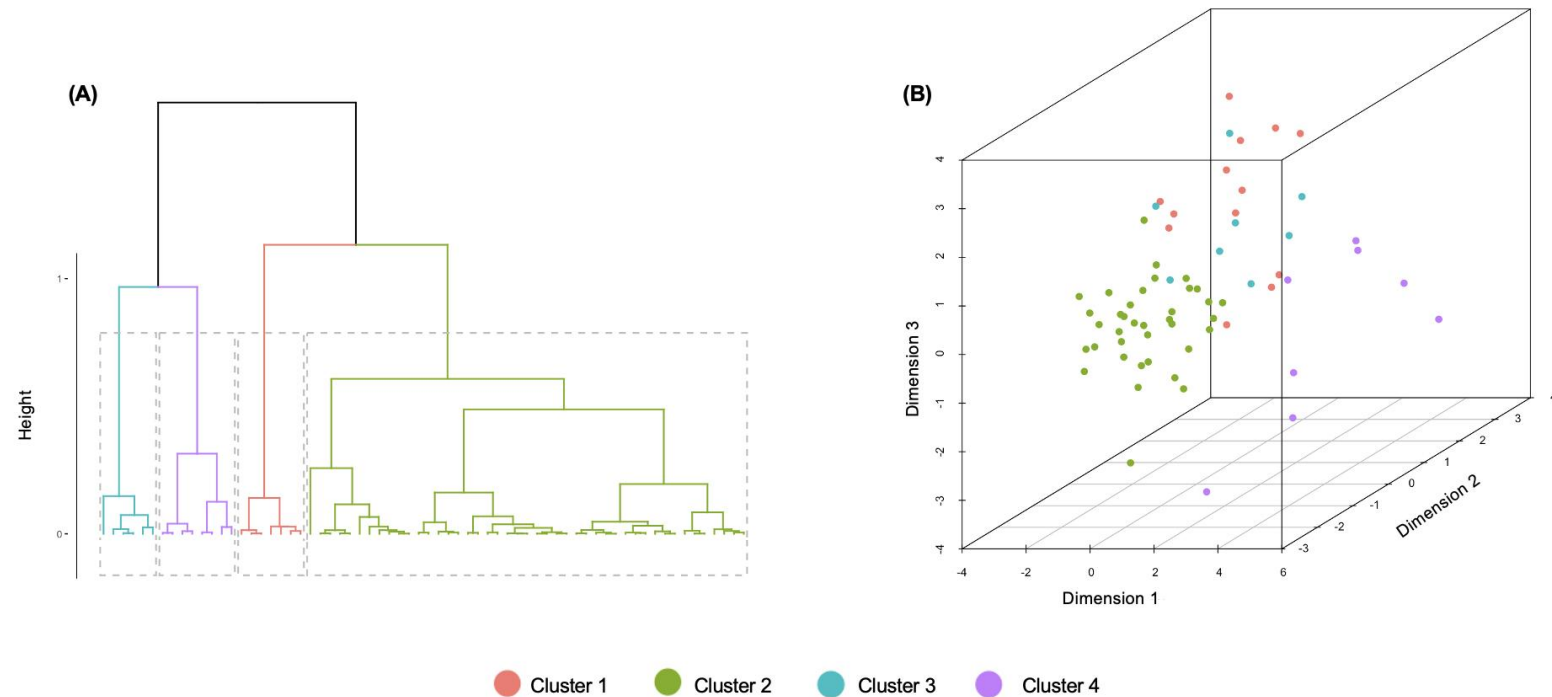


3 Neuroinflammation



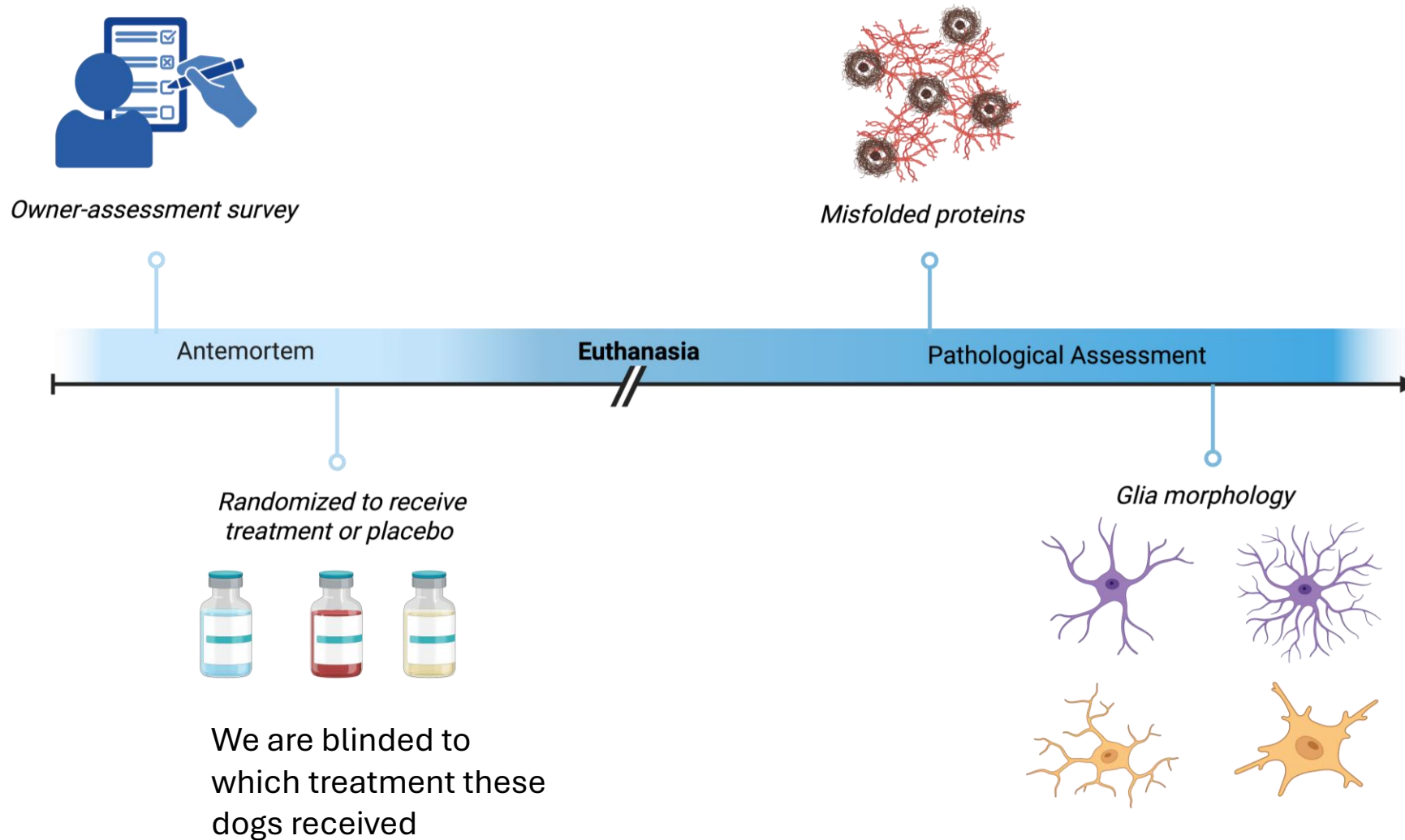
Aging dogs cluster into pathological phenotypes

- 59%: little to no pathology
- 12%: Astrocyte activation and tau pathology
- 8%: $A\beta$ and tau pathology with higher microglial and astrocyte activation
- 8%: $A\beta$ slightly stronger than #3, lower glial activation but no tau pathology

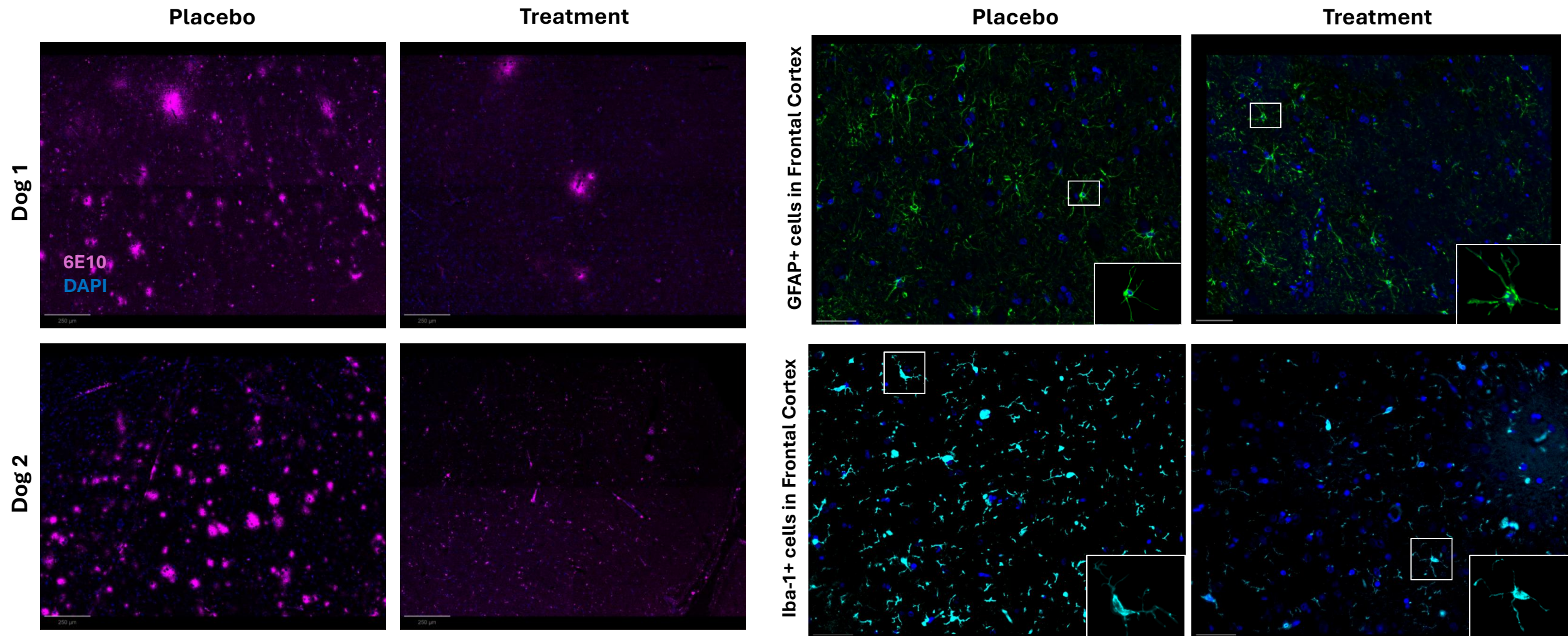


Most severe pathology: 67% are female

Therapeutic intervention



Treatments mitigate amyloid plaques density and glial inflammation



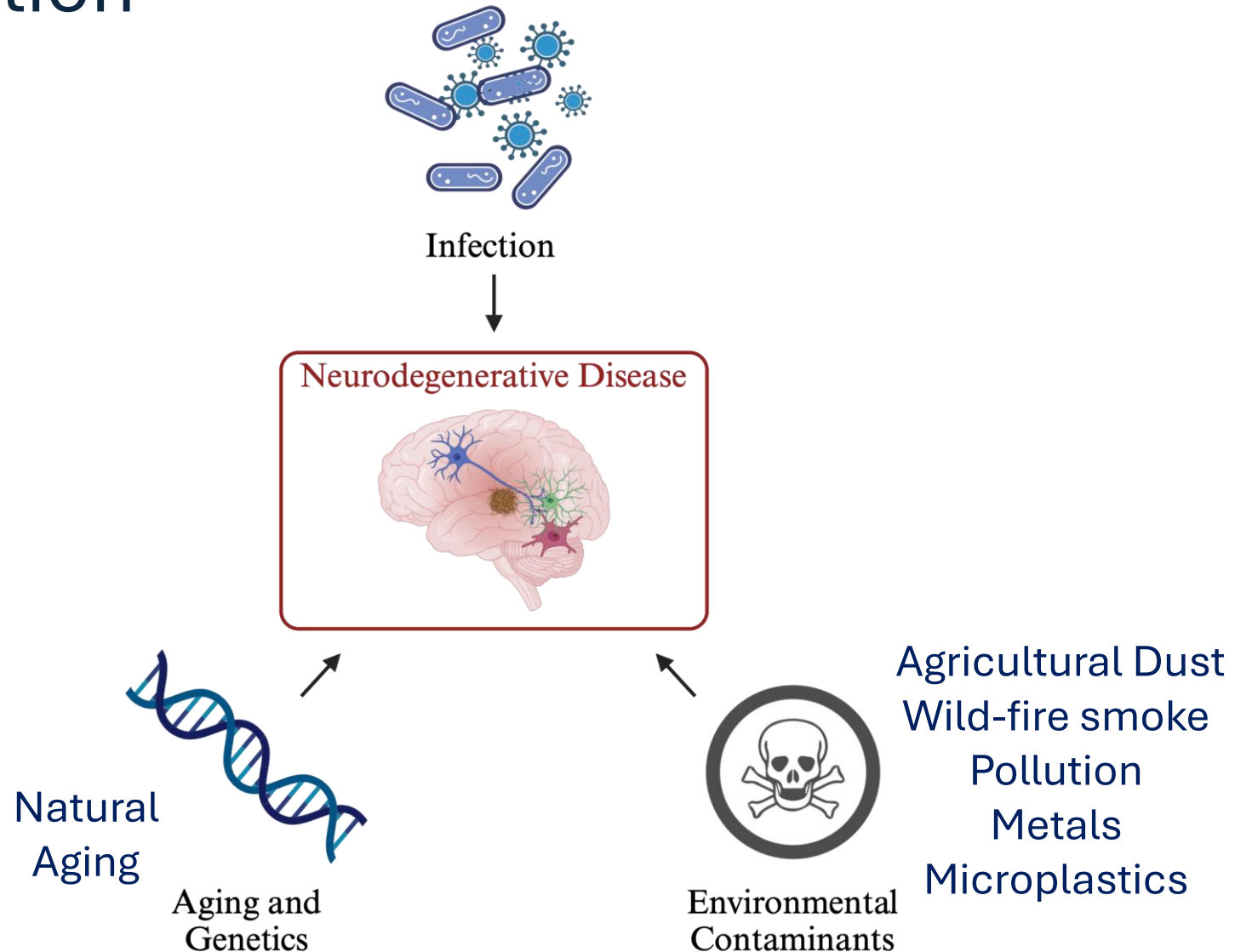
Conclusions so far:

- Common biomarkers as possible diagnostics
- Canines as a naturally aging model with AD-like pathology, CCD
- Preliminary neuroinflammation and disruption of BBB is occurring as toxic pathological proteins accumulate
- Preliminary data show that treatments prevent increased A β -plaque density and neuroinflammation in a small cohort compared to placebo



Risk factors and exposures during a lifetime can play a role in neurodegeneration

- Can follow over lifetime
- Better understand the cell signaling events
- Current clinical trials



Acknowledgments

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Columbine Health Systems
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**Dog Aging
Project**

Longer, healthier lives. Together.



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