Gut microbiota analysis of an Alzheimer’s Disease transgenic rat model

Kristin A. Zabrecky1; Daniel J. Davis2; Elizabeth C. Bryda2

1The Ohio State University College of Veterinary Medicine, Columbus, OH; 2Rat Resource and Research Center, Department of Veterinary Pathobiology, College of Veterinary Medicine, University of Missouri, Columbia, MO

Background

• Alzheimer’s Disease (AD) is the leading cause of dementia in the growing elderly population.1
  • A new transgenic rat model, F344-Tg(Prp-APP;Prp-PS1)19(Rcr) (TgF344-AD), carries two mutations, amyloid beta (Aβ) precursor protein (APP) and human Presenilin 1 (PS1), both associated with familial AD.2
  • The TgF344-AD rat strain has been previously shown to have a phenotype more representative of human disease than existing rodent models.2
  • There is growing evidence for the role and interaction of the gut microbiota in neurodegenerative disease progression.3

Hypothesis

Neuropathological and behavioral changes in TgF344-AD rats will have accompanying microbiota alterations with increasing disease severity and age.

Methods

Microbiota Analysis

Characterization of AD Phenotype

Proposed Sequence for Familial AD

Representative group of AD (n=6) and wildtype (WT) (n=4) male rats of varying ages underwent behavioral testing, brain histology, immunohistochemistry (IHC), and quantitative polymerase chain reaction (qPCR).

Behavioral Testing

Open field test

Novel object preference

Immunohistochemistry and Histology

Amyloid β

Tau

qPCR

Alzheimer’s Disease Phenotype

Analysis

Summary and Future Directions

• Although there was no difference in the microbiota among age groups, a significant difference was seen between male and female TgF344-AD rats of all ages.
  • The AD phenotype was consistent with previous studies. We noted an unexpected decreased activity level in the AD rats in the open field behavioral test.2
  • Future studies with comparisons to unaffected litter mates are needed to confirm the microbiota results.

References and Acknowledgements


This project was funded by American Society of Laboratory Animal Practitioners Foundation, GlaxoSmithKline, IDEXX-BioResearch (K24) and NH SP40 CD011602 (ECB). We thank the entire Bryda and Amos-Landgraf laboratories in the Department of Veterinary Pathobiology, Suheil Saeed, Ali Hansen, Dr. Marita Hart, Dr. Craig Frindt, and Dr. Cynthia Beach-Wilden.