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Alzheimer's research using animal models significantly increases understanding of the disease

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Very few species spontaneously develop the cognitive, behavioral and neuropathological symptoms of Alzheimer's disease (AD), yet AD research must progress at a more rapid pace than the rate of human aging. Therefore, in recent years, a variety of animal models have been created – from tiny invertebrates with life spans measurable in months to huge mammals that live several decades. A special issue of the *Journal of Alzheimer's Disease* (December 2008), assembled by guest editor Diana S. Woodruff-Pak, Temple University, Philadelphia, explores the variety of animal models now being used in AD research and the resulting therapeutic implications.

"Because of the rare instances of spontaneous development of AD pathology in non-human species, animal models have been developed using various genetic, biochemical, or dietary manipulations to approximate full-blown symptoms of the disease," commented Dr. Woodruff-Pak.

"The purpose of this Special Issue of the *Journal of Alzheimer's Disease* (*JAD*) is to provide an overview of the available animal models of AD and to highlight the power of these models in elucidating mechanisms and treatments. To bridge the wide gap between the molecular biology of AD and clinical therapeutics, it is essential to have valid non-human animal models to investigate disease mechanisms, test treatments, and evaluate preventative strategies and cures. While each animal model has

limitations, the value of animal models for research on AD is immeasurable. Our progress in establishing a knowledge base about AD would be slowed, and in some cases prevented, without animal models."

Bringing together 13 contributions from worldwide experts, the models span the fruit fly, mouse, rat, rabbit, dog and non-human primate species. Dr. Woodruff-Pak, in an introductory article, describes the advantages and unique characteristics of each of these models.

The fruit fly model is discussed in an article by Iijima and Iijima-Ando where associative learning and memory can be assessed by olfactory conditioning and can be used to model impairment of human patients with AD. In a contribution by Khurana, the fruit fly can be used to model tau-dependent neurodegeneration, a hallmark of AD and related neurodegenerative disorders.

Wilcock and Colton describe the mouse studies of anti-amyloid-β immunotherapy and how they relate to clinical trials, while the role of estrogen in normal aging and AD is addressed by Foy and associates. Behavioral consequences of tau overexpression are described by Morgan and his group. The article by Pallas and colleagues presents the senescence-accelerated prone mouse strain 8 (SAMP8) as a model of early AD and mild cognitive impairment. Two new transgenic mouse models of AD are described by Colton and her colleagues. As described above, these mice progress through a number of stages of AD in a manner that parallels the disease in humans.

Begum has tested amyloid-β infusions in the rat and describes ways to accelerate the effects so that results can be obtained more quickly and efficiently.

Three articles discuss the cholesterol-fed rabbit as a model for various processes in AD. Sparks discusses how cholesterol in the diet causes

accumulation of amyloid-β, whereas copper introduced in the drinking water impairs elimination of amyloid-β. Coico and Woodruff-Pak discuss the eyeblink response in rabbits, a form of associative learning that is severely impaired in AD, and which can be affected by excess cholesterol in the diet. An article by Ghribi demonstrates that feeding rabbits over a long time period with cholesterol causes an increase in the cholesterol content in neurons, which in turn can cause an accumulation of amyloid-β in the brain.

The article by Cotman and Head describes two decades of research with canines as models of normal aging and AD. They provide a summary of the beneficial effects of an antioxidant diet, behavioral enrichment, and amyloid-β immunotherapy.

Finally, the article by Buccafusco documents the numerous preclinical trials that have been carried out in his laboratory using non-human primates to identify cognition-enhancing drugs to treat AD.

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