HANDBOOK OF ANIMAL MODELS IN ALZHEIMER’S DISEASE
Advances in Alzheimer's Disease

Advances in Alzheimer's Disease brings together the latest insights in Alzheimer’s disease research in specific areas in which major advances have been made. This book series assembles and builds on work recently published in the Journal of Alzheimer's Disease (JAD) and also includes further contributions to ensure comprehensive coverage of the topic. The emphasis is on the development of novel approaches to understanding and treating Alzheimer’s and related diseases.

Series Editors:
George Perry, Ph.D. and Mark A. Smith, Ph.D.†

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Handbook of Animal Models in Alzheimer’s Disease

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Dedication

This handbook is in honor and memory of my husband and colleague, Mark A Smith, who tragically passed away on December 19, 2010. With his death, Mark left a huge void in the field of neurodegeneration but also left an incredible legacy to look up to and carry forward.

Mark was an incredibly prolific investigator and a significant contributor to the field of Alzheimer’s disease. In just 20 years, he rose to become one of the most highly cited scientists in the field, authored over 800 publications, was honored with a multitude of prizes, and served on a number of editorial boards, meetings, and organizations. Scientifically, he gave the field of Alzheimer’s disease and neurodegeneration seminal insights on the role of oxidative stress and cell cycle re-entry in AD pathogenesis. However, beyond these remarkable achievements, Mark will also be remembered for his tireless fight to challenge those around him to examine data from all possible angles, to not fall in line with the popular dogma but to try to disprove it. In other words, to do what science stands for at its core. He will be remembered as a creative and generous scientist who thought outside of the box, and through his zest for life and passion for his work, for his ability to deliver to audiences around the world what no one else could. His fearless approach to science has taught the field to keep our eyes on the future and to not sit too long on what is known, to question incessantly, and to keep pushing ahead. To those close to him, he emphasized the importance of generosity, collaboration, and teaching to promote the careers of the next generation. He infected everyone with the same fun, curiosity, and excitement for doing science that he carried inside him and the courage and freedom to stand true to one’s convictions. To me, he has left the amazing love, strength, and knowledge that he gave me every day and SO many laughs to remember him by to continue on this journey. To his sons, he has left freedom and fortitude in their spirits to follow their hearts as they grow and a ferocious love for soccer.

It is so cruel to see such a bright light burn out so fast, but he has left a mark in all of us and with that the duty to be true to ourselves and to give our best to cure this devastating disease.

Gemma
Preface

References of experimental use of animals to model diseases, novel experimental procedures, or test novel therapeutics date all the way back to 304–258 BCE. It is undisputable that our ability to model disease in animals has provided major breakthroughs in all fields of biomedical research and has been vastly accelerated by the development of transgenic animals.

The study of neurodegenerative diseases is highly reliant on animal models due to their complexity and plurality of pathology and symptomatology. Today we have amassed a multitude of animal models, developed through genetic, chemical, and/or lesions in multiple species with the goal of faithfully mimicking these diseases and uncover the complex nature of disease-associated mechanisms. Ultimately, the goal is to test promising therapies and manage, prevent, or cure neurodegenerative disease.

The field of neurodegenerative diseases faces unique challenges in this application. First, most animal models in this area, unlike in linear diseases, do not reproduce the full phenotypical disease spectrum. Second, for a given neurodegenerative disease, the etiology and the clinical presentation differ from one patient to the next. As such, while the current models are well suited for the study of specific pathology-driven mechanisms, more notably amyloid-β, tau, or alpha-synuclein, pharmacological testing in animal models of neurodegenerative disease often translates into poorer indices of efficacy when applied to the clinical population. With these advances and challenges in mind, this handbook, written by experts in the field of neurodegeneration, provides a rich and updated overview of a wide range of animal models that are being developed and used to study complex disease dynamics, including but also beyond pathology-associated mechanisms, with the ultimate goal to discover the neuroprotective therapeutics of the future through more accurate translation of basic to clinical outputs.

The first section of this handbook presents an overview of animal models of various species, ranging from higher mammals such as primates or dogs, to knowledge gathered for more prevalent rodent genetically-based models, as well as promising models developed in the rabbit to study metabolic endpoints and therapeutic strategies for AD. Last but not least, this first section includes the review of newer invertebrate animal models, such as Drosophila to study neurodegeneration. Invertebrate models provide high-throughput potential, with highly manipulable genetics and functional output that places these models in promising standing within the field.

The second section of this handbook presents the use of animal models to pinpoint disease mechanisms. Pathology driven mechanisms are well represented but not limiting. As we are learning that “bottom-up”, over-expression based transgenic models do not provide an accurate representation of therapeutic effectiveness, we have also focused on more “top-down” models, for example those based on metabolic pathological endpoints that exclude pathology as the primary driver of neurodegenerative disease.

Lastly, this handbook concludes with a representation of various therapeutic interventions that are being used in models of neurodegenerative disease. Critical insight on effectiveness of clinically tested therapies in addition to novel, untested ones are aimed at providing both, the necessary critical due diligence when treatments fail – “where have we gone wrong” – “How can we do better” and a glimpse of hope for the future.

The Editor
The contributions in this book are based on articles previously published by IOS Press in the *Journal of Alzheimer’s Disease*, and have in most cases been revised and updated.
Contents

Preface vii

Section 1. Overview of Animal Models of Alzheimer's Disease

Estimation of Working Memory in Macaques for Studying Drugs for the Treatment of Cognitive Disorders
Jerry J. Buccafusco 3

The Canine Model of Human Aging and Disease
Carl W. Cotman and Elizabeth Head 15

Unveiling “The Switch” from Aging to Alzheimer’s Disease with the Senescence-Accelerated Mouse Model (SAMP8)
Jaewon Chang, Merce Pallas, Xiongwei Zhu, Hyun-Jin Kim, Antoni Camins, Hyoung-gon Lee, George Perry, Mark A. Smith and Gemma Casadesus 39

Alzheimer’s Disease Selective Vulnerability and Modelling in Transgenic Mice
Jürgen Götz, Nicole Schonrock, Bryce Vissel and Lars M. Ittner 49

The Cholesterol-Fed Rabbit as a Model of AD: The Old, the New and the Pilot
D. Larry Sparks 59

A Rabbit Model of Alzheimer’s Disease: Valid at Neuropathological, Cognitive, and Therapeutic Levels
Diana S. Woodruff-Pak, Alexis Agelan and Luis Del Valle 77

Transgenic Drosophila Models of Alzheimer’s Amyloid-β 42 Toxicity
Koichi Iijima and Kanae Iijima-Ando 89

Section 2. Using Animal Models to Understand Mechanisms of Disease

Estrogen, Progesterone and Hippocampal Plasticity in Rodent Models
Michael R. Foy, Michel Baudry, Roberta Diaz Brinton and Richard F. Thompson 109

Apparent Behavioral Benefits of Tau Overexpression in P301L Tau Transgenic Mice
Dave Morgan, Sanjay Munireddy, Jennifer Alamed, Jason DeLeon, David M. Diamond, Paula Bickford, Michael Hutton, Jada Lewis, Eileen McGowan and Marcia N. Gordon 129

Activation of Cell Cycle Proteins in Transgenic Mice in Response to Neuronal Loss But Not Aß and Tau Pathology
Joao P. Lopes, Mathew Blurton-Jones, Tritia R. Yamasaki, Paula Agostinho and Frank M. LaFerla 139

Electron Microscopic 3D Reconstruction Analysis of Amyloid Deposits in 3xTg-AD Mice and Aged Canines
Paworn Nuntagij, Naiphinich Kotchabhabkdi and Reidun Torp 149
Section 3. Alzheimer's Disease Therapies Using Animal Models

Developing Immunotherapies for Alzheimer’s Disease Using a Cholesterol-Fed Rabbit Model in the Context of Th cell Differentiation
  Richard Coico and Diana Woodruff-Pak

Anti-Amyloid-β Immunotherapy in Alzheimer’s Disease: Relevance of Transgenic Mouse Studies to Clinical Trials
  Donna M. Wilcock and Carol A. Colton

Heterogeneity in Red Wine Polyphenolic Contents Differentially Influences Alzheimer’s Disease-Type Neuropathology and Cognitive Deterioration
  Lap Ho, Ling Hong Chen, Jun Wang, Wei Zhao, Stephen T. Talcott, Kenjiro Ono, David Teplow, Nelson Humala, Alice Cheng, Susan S. Percival, Mario Ferruzzi, Elsa Janle, Dara L. Dickstein and Giulio Maria Pasinetti

Delivery of NGF to the Brain: Intranasal Versus Ocular Administration in Anti-NGF Transgenic Mice
  Simona Capsoni, Sonia Covacevszach, Gabriele Ugolini, Francesca Spirito, Domenico Vignone, Barbara Stefanini, Gianluca Amato and Antonino Cattaneo

Cholinomimetic Actions of Memantine on Learning and Hippocampal Plasticity
  Benjamin Drever, William Anderson, Helena Johnson, Matthew O’Callaghan, Sangwan Seo, Deog-Young Choi, Gernot Riedel and Bettina Platt

Cognitive Performances of Cholinergically Depleted Rats Following Chronic Donepezil Administration
  Debora Cutuli, Francesca Foti, Laura Mandolesi, Paola De Bartolo, Francesca Gelfo, Daniela Laricchiuta and Laura Petrosini

Subject Index

Author Index