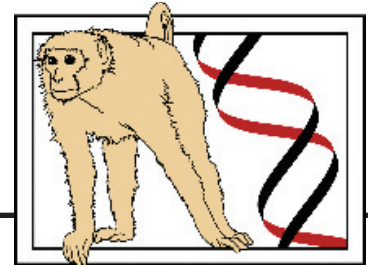


Aging & Regenerative Medicine

Wisconsin National Primate Research Center

University of Wisconsin-Madison



The National Primate Research Center at the University of Wisconsin-Madison is home to the world's largest collection of well characterized elderly rhesus monkeys. This colony is supported in part by a special supplement to the base operating grant from the National Institute on Aging (NIA).

The center has strong ties to the NIA, the UW Institute on Aging, and the UW Departments of Medicine, Kinesiology, Ophthalmology, Neuroscience, Physiology, Nutritional Science, Ob/Gyn, Veterinary Science, Zoology, Psychology, Cell and Molecular Biology and Developmental Biology.

Following are Primate Center studies related to aging:

CALORIC RESTRICTION AND AGING

Ongoing research since 1987 on calorie-restricted rhesus monkeys has revealed that the restricted animals are healthier than their age-matched controls. They show better glucoregulation and lower incidence of diabetes, favorable changes in plasma lipids and less risk for cardiovascular disease, and less incidence of osteoarthritis. Most of them even appear younger looking than the controls.

The studies are led by **Richard Weindruch** at the Institute on Aging. He and others are investigating diseases of aging and the normal aging process with the aim of understanding, treating and preventing age-related diseases.

Joseph Kemnitz and **Ricki Colman** at the Primate Center, along with their many collaborators, are learning more about the biological mechanisms that control food intake and energy expenditure. They have found that aging rhesus monkeys are excellent models for studying obesity, diabetes, hypertension, coronary heart disease, osteoporosis, osteoarthritis, neural function, menopause, endometriosis and other conditions and disorders.

AGING AND REGENERATIVE MEDICINE

Embryonic stem cell research is bringing us closer to the possibility that we may be able to transplant healthy cells into diseased human tissues without immune system rejection.

The breakthrough derivation and culture of human embryonic stem cells (ES cells) by **James Thomson** and his team at the UW-Madison evolved from his extensive experience working with rhesus monkey ES cells since the early 1990s.

Research with monkey stem cells continues at the Primate Center. Any human stem cell-based therapies will be novel and require extensive testing to demonstrate safety and efficacy. The rhesus monkey and rhesus ES cells provide an appropriate model for developing new transplantation therapies.

UW-Madison and WNPRC scientists have derived blood, neural, cardiac and pancreatic cells from rhesus ES cells. Transplantation of embryonic stem cell or induced pluripotent stem cell derivatives in rhesus monkeys could help develop treatments for leukemia, Parkinson's disease, heart disease, diabetes, and other diseases that can strike at any age, and are increasingly afflicting aging individuals.

PARKINSON'S DISEASE

Primate Center researchers are exploring avenues for potentially treating patients with Parkinson's disease.

Marina Emborg, WNPRC Senior Scientist, is researching Parkinson's in nonhuman primates. She has studied preclinical models for Parkinson's therapies, and has analyzed methods of cell transplantation and gene therapy for Parkinson's. She has been part of seminal work on gene therapy for the delivery of glial derived neurotrophic factor (GDNF) in nonhuman models of Parkinson's Disease. She is the scientific director of the Primate Center's Preclinical Parkinson's Disease Research Program, established in 2006. She collaborates with stem cell scientists Clive Svendsen and Su-Chun Zhang at the Waisman Center.

Erwin Montgomery, Neurology, is researching deep brain stimulation (DBS) as a method for treating symptoms of Parkinson's Disease. DBS is proving effective in reversing the symptoms of Parkinson's Disease in some, but not all patients. The therapy involves implanting a modified electronic cardiac pacemaker into the chest, and connecting this stimulator to electrodes implanted deep within the brain. However, researchers are not certain why it works in some people and not in others. More knowledge gained from nonhuman primate studies using this electrical, versus pharmaceutical approach to treating Parkinson's may help doctors help more patients with this and other neurological conditions in the future.

MITOCHONDRIAL DNA ABNORMALITIES AND SARCOPENIA

Judd M. Aiken has studied mitochondrial involvement in the aging process. He has helped elucidate the role that mitochondrial DNA abnormalities play in aging. The mitochondrion provides an essential energy source to cells, yet its genome is susceptible to damage with age. Aiken and his team have been examining the mitochondrial genome for age-associated changes such as sarcopenia (muscle-loss) as well as the effects these alterations produce. They have identified an accumulation of mitochondrial DNAs containing large deletions in aging mice, rats and rhesus monkeys.

MARMOSETS AS A MODEL FOR OSTEOPOROSIS

Mark Dresner, David Abbott, Ricki Colman and **Wendy Saltzman** are studying common marmosets as a model for osteoporosis research. Socially subordinate female marmosets show sustained low levels of estrogen. Yet, as they age, they do not suffer from accompanying bone loss as do human females with low estrogen. In marmosets, the low estrogen levels accompany low cortisol levels typical of females whose ovulation is suppressed.

HIGH DIETARY VITAMIN A

Sherry Tanumihardjo, Nutritional Sciences, and **Kristina Penniston**, Surgery, have examined Vitamin A intake in rhesus and marmoset monkeys to not only improve animal health but to show how susceptible humans may be to toxicity from consuming too much Vitamin A. They have revealed subtoxic liver concentrations of Vitamin A in monkeys fed common research diets. They are also developing ways to more accurately measure the amount of Vitamin A in the body, to help combat not just Vitamin A excess (e.g., through vitamin supplements and fortified food) but also deficiency.

OCULAR AGING

Paul Kaufman, Ophthalmology and Visual Sciences, has developed new compounds to enhance aqueous outflow from the eye and treat glaucoma, which afflicts about 3 million women and men in the U.S. The rhesus monkey is an invaluable model for studying glaucoma, the second most common cause of irreversible vision loss among Americans and the most common among African Americans. The most common form of the disease, open-angle glaucoma, is strongly age-dependent. The prevalence among those over age 70-75 is five percent in Caucasians, 10-12 percent in African Americans, and 20-25 percent in Afro-Caribbeans. Kaufman has focused on novel compounds and gene therapeutic

strategies to enhance fluid drainage from the eye, and on other compounds to protect retinal ganglion cells and their axons from pressure-induced damage.

Another finding is that presbyopia, or the progressive loss of ability to focus as we age, is not caused solely by changes in the lens, but also potentially by changes in the ciliary muscle. Stiffening of this muscle and its posterior attachments with age restricts its movement which, due to its attachments to the lens, may prevent the lens from changing shape and properly focusing. The restriction of ciliary movement could contribute to glaucoma as well as presbyopia since the muscle also has attachments in the eye's fluid outflow pathways. Reduced agitation of these pathways caused by ciliary muscle microcontractions could allow material to build up in the pathways, restricting flow and contributing to elevated intraocular pressure. The rhesus monkey is a model for presbyopia pathophysiology and for testing new intraocular lenses that may have the capability of restoring accommodation as well improving visual clarity when replacing cataractous lenses.

OBESITY RESEARCH

Joe Kennnitz, Physiology and WNPRC Director, is collaborating with several scientists on obesity research. They are evaluating in rhesus monkeys the effects of administering certain peptides recently identified to regulate appetite and feeding behaviors. They are also evaluating feeding and metabolism in rhesus monkeys in response to chemical or electrical stimulation of the hypothalamus. The hypothalamus plays a critical role in regulating appetite and energy balance. The long-term aim is to reduce obesity and ameliorate its harmful health consequences.

PRIMATE AGING DATABASE

In 2005, the WNPRC launched the Internet Primate Aging Database, a resource of primate biomarkers of aging to improve collaborative research and treatment efforts related to diseases and disorders of aging:

<http://ipad.primate.wisc.edu/>

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