

The Essential Need for Animals in Medical Research

Introduction

Less than ¼ of one percent of all lab animals used in the U.S. are non-human primates. Approximately 30 different species are studied by the research community.¹ Many historic scientific breakthroughs, such as the discovery of the Rh factor and the development of a live polio virus vaccine were achieved through research with non-human primates. Today they are considered extremely important models in many areas of medicine because of their close relationship to humans.

AIDS — Acquired Immune Deficiency Syndrome

Scientists face major challenges in their quest to develop a vaccine for human immunodeficiency virus (HIV), the agent that causes AIDS. Having no human model of protection to guide them, medical researchers depend heavily on monkeys for the development of promising strategies to protect people from this disease. Vaccines containing various strains of a simian immunodeficiency virus (SIV), a closely related virus that follows a disease course similar to HIV, or a hybrid human/simian immunodeficiency virus (SHIV) are being tested in macaque monkeys, and several research groups have successfully vaccinated monkeys with viral preparations that reduce

viral load and halt disease progression. If these results can be generalized to humans, the vaccines may be used to treat HIV-infected persons.²

Hepatitis B and C

Chimpanzees are uniquely susceptible to human hepatitis virus infections and serve as an important study model for this global public health problem. Research with chimpanzees has virtually eradicated hepatitis B and C infections acquired through blood transfusions, a landmark achievement in the control of viral hepatitis. Commercially available hepatitis B vaccines have prevented the development of cirrhosis and liver cancer in millions of people. Because no vaccine for hepatitis C infections is yet available, scientists continue to study the pathogenesis of this disease in chimpanzees to gain a better understanding of the infection process, to improve current treatment modalities, and to pave the way for the development of an effective vaccine.^{3, 4}

Malaria

Researchers are beginning to overcome some of the enormous obstacles in developing a vaccine against malaria, a disease that effects millions of people annually. New-world monkeys and chimpanzees are the only species suitable for vaccine evaluation because they are susceptible to the same strains of the parasites that cause human malaria.

Unlike simpler organisms, the malaria parasite has many chromosomes, thousands of genes, and a four-stage life cycle as it passes from mosquitoes to humans and back again. A number of promising vaccines that attack the organisms at every vulnerable point in its life cycle are being tested. Some of these have successfully stimulated protective responses in animals and may soon be ready for human trials.⁵

Acute Respiratory Disease

Respiratory syncytial virus (RSV) can cause life-threatening respiratory infections in infants, young children and the elderly. Since there is no effective therapy, an RSV vaccine is a high medical priority in the U.S. Researchers are designing vaccines containing live, weakened viruses that are suitable for applying with nose drops. These vaccines are being tested for their ability to protect chimpanzees, the only animal that is naturally infected by RSV and develops an illness with symptoms similar to those seen in humans.⁶

Periodontal Disease

Microbial infection of the tissue supporting teeth is the most common cause of bone and tooth loss in humans and may be an important risk factor for cardiovascular disease. Periodontitis is also a health problem for captive primates,

making these species excellent models for studying the connection between chronic oral infections and systemic disease. Several groups of researchers have shown that immunizing monkeys with a vaccine containing a killed oral bacterium can halt infection and suppress bone loss.⁷

Aging and Nutrition

Scientists are currently studying the effects of long-term calorie restriction (CR) on the biology of aging in macaque monkeys. They have learned that a reduction in calories over a period of several years lowers body temperature, slows metabolism, lessens the risk of cardiovascular disease, and reduces predisposition toward diabetes. Long-term studies of CR have increased the life span of monkeys.⁸

Brain Biology

Because they share many features of brain biology and structure with humans, non-human primates are extremely valuable models for studying normal brain function and brain-related diseases, including mental, neurological, and addictive disorders. Many of the functional regions of the cerebral cortex that are present and identifiable in monkeys and other small primates have provided a precise map of the brain circuitry involved in visual and auditory perception, learning and memory deficits, and brain and spinal cord injuries.⁹

Alzheimer's Disease

The decline of memory and other mental functions in patients with Alzheimer's disease (AD) is associated with the loss of or damage to cholinergic nerve cells that use the chemical acetylcholine to transmit messages to other cells in the brain. Age-related reduction in the functions of these nerve cells also occurs in primate species. Scientists have shown that grafting genetically modified cells to produce nerve growth factor (NGF) directly into the brains of macaque monkeys is a safe procedure that enhances the survival and function of the cholinergic nerve cells. Such studies are now being extended to humans in an attempt to slow the loss of memory in patients with AD.¹⁰

Parkinson's Disease

Parkinson's disease (PD) is a slow, progressive disease, generally found in the aged, that is characterized by tremors. Scientists know that the disease is associated with degeneration of brain cells that produce a chemical (neurotransmitter) called dopamine. Recently, they found a new method to deliver the gene that produces GDNF (a factor that protects brain cells) directly into the brains of monkeys. The treatment successfully prevented the progression and reversed the symptoms of PD. Clinical testing to forestall human disease is under consideration.¹¹

References

1. Sibal LR, Samson KJ. 2001. Nonhuman primates: a critical role in current disease research. *ILAR J* 42:74-84.
2. Nathanson N, Mathieson BJ. 2000. Biological consideration in the development of a human immunodeficiency virus vaccine. *J Infect Dis* 182:579-589.
3. Prince AM, Brotman B. 2001. Perspectives on hepatitis B studies with chimpanzees. *ILAR J* 42:85-88.
4. Alter MJ, Seeff LB. 2000. Recovery, persistence, and sequelae in hepatitis C virus infection. *Semin Liver Dis* 20:17-35.
5. James S, Miller L. 2000. NIAID (National Institute of Allergy and Infectious Diseases, NIH). *Malaria Vaccine Development: Status report*. Washington, DC: GPO.
6. Collins PL et al. 1999. Rational design of live-attenuated recombinant vaccine virus for human respiratory syncytial virus by reverse genetics. *Adv Virus Res* 54:423-451.
7. Persson GR et al. 1994. *Macaca fascicularis* as a model in which to assess the safety and efficacy of a vaccine for periodontitis. *Oral Microbiol Immunol* 9:104-111.
8. Hansen BC et al. 1999. Calorie restriction in nonhuman primates: mechanisms of reduced morbidity and mortality. *Toxicol Sci* 52:56-60.
9. Newsome WT, Stein-Aviles JA. 1999. Nonhuman primate models of visually based cognition. *ILAR J* 40:78-91.
10. Merrill DA et al. 2000. Conservation of neuron number and size in entorhinal cortex layers II, III, and V/VI of aged primates. *J Comp Neurol* 422:396-401.
11. Kordower JH et al. 2000. Neurodegeneration prevented by lentiviral vector delivery of GDNF in primate models of Parkinson's disease. *Science* 290:767-773.