

## *The Essential Need for Animal Models in Medicine and Basic Research:*

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### Introduction

Less than ¼ of one percent of laboratory animals in the US are non-human primates (1), and most of these animals are lower-order primates (i.e. monkeys, not chimpanzees or other great apes). **Many historic scientific breakthroughs have come from research on lower-order primates, including the discovery of Rh factor (from rhesus monkeys), which allowed safe blood transfusions, and the development of vaccines for polio and yellow fever.** Today, monkeys are considered extremely important models in many subfields of biomedical research, including HIV, malaria, stem cell research, neurology, psychiatry, dentistry, and obstetrics. Additionally, lower-order primates are a valuable non-rodent model for toxicity testing, and are required in the drug approval and environmental protection processes to help prevent public health disasters (2).

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### HIV/AIDS

The similarity between human and monkey immune systems make lower-order primates useful models for acquired immunodeficiency syndrome (AIDS) research (3, 4). The CDC estimates that human immunodeficiency virus (HIV), the cause of AIDS, infects 1.1 million Americans. However, thanks to therapeutic methods discovered because of research done on monkeys infected with simian immunodeficiency virus (SIV), HIV is no longer an impending death sentence, but a manageable condition (3, 5). Today, work on lower-order primates continues to expand our understanding of how HIV persists in the body during antiviral treatment and facilitates the development of new HIV treatments that can improve life expectancy and quality of life for HIV positive individuals (5, 6).

Additionally, research on lower-order primates is crucial to the struggle to develop an HIV vaccine. Non-human primate models are necessary to understand the mechanism of protection (how the vaccine works), and determine the relative efficacy of different vaccine

strategies in order to improve current vaccine approaches and select the most promising candidates for phase III trials in humans (4, 7).

### Alzheimer's & Parkinson's

Because they share many features of brain biology and structure with humans, non-human primates are valuable models for studying brain function and neurological diseases. Research with non-human primates is contributing to our knowledge of the cause of, and the effectiveness of proposed treatments for, Alzheimer's disease, a neurodegenerative disease that affects over 4 million Americans (8, 9). Non-human primates are also valuable in research on Parkinson's disease, a neurodegenerative disease that can impair movement and cognitive function. A recent review article published in a leading medical journal credited neurological studies in monkeys with starting a renaissance in Parkinson's disease research and spurring the development of new treatments such as dopamine agonists (10).

### Stem Cells

In the promising field of stem cell research, a major barrier is the efficiency of gene transfer, which partially accounts for the current therapeutic ineffectiveness of stem cells. Researchers are using rhesus monkeys to gain a greater understanding of gene transfer in order to solve the problem, so that gene therapy using stem cells can achieve its potential to improve treatment for various genetic, cancerous, and infectious diseases (11). This is but one example of how lower-order primate models are critical to the advancement of stem cell research and the development of useful human stem cell therapies.

### Birth Defects

Research on marmoset monkey embryos greatly contributed to our understanding of the tragic effects of thalidomide (12). Before a public health disaster occurs, many biologically active compounds that have been

shown to cause teratogenesis (birth defects) in other species, are first evaluated in monkeys to discover if they could potentially cause birth defects in humans. Lower-order primates are also used to study Fetal Alcohol Syndrome (FAS). Thus, research on lower-order primates is critical in preventing birth defects and reducing the infant mortality rate.

## Mental Disorders

The understanding of the brain's neural circuits gained through basic biomedical research on monkeys led to the development of targeted surgical ablation and deep-brain stimulation (10). Deep-brain stimulation, a treatment in which implanted electrodes emit electric pulses to keep neurons operating properly, has been revolutionary in not only treating Parkinson's but also mental disorders. Furthermore, forms of affective disorders, such as Major Depression and Tourette syndrome, and anxiety disorders, like Obsessive Compulsive Disorder, that were formerly thought resistant to all available therapies can now be treated using deep-brain stimulation, which was pioneered in lower-order primates (8).

Moreover, work on lower-order primates was vital to the development of revolutionary brain-computer interfaces that improve quality of life for fully paralyzed patients by allowing them to use a computer or drive a wheelchair using only their thoughts (13). Scientific miracles are usually built on a foundation of basic biomedical research and revolutionary concepts are often proved feasible in primate models.

## Malaria

The search for a vaccine against malaria, a blood disease that infects over 350 million people annually, is dependent on the use of lower-order primates in biomedical research. New-world monkeys (along with chimpanzees) are the only species susceptible to the same strains of malaria parasites as humans, and thus the only suitable models for vaccine evaluation. In a demonstration of how biomedical research on lower-order primates continues to yield results in the battle against malaria, the authors of a March 2009 paper confirmed the possibility of using a recombinant protein

as a vaccine against the *P. vivax* strain of malaria by conducting trials on lotus monkeys (14).

## Toxicity Testing

Primates remain important for testing the toxicity of new drugs before they are administered to human volunteers (preclinical testing). The standard regimen includes testing at various doses on a rodent model and a non-rodent model, which is sometimes a nonhuman primate, for at least two weeks. A review in the journal of Toxicology and Pathology concluded that this regimen works most of the time, and any failures of the animal modeling to predict human toxicity have been due to specific and rare biological phenomena (2).

## 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 (15). Periodontitis is also a health concern for captive primates, making these species excellent models for studying the connection between chronic oral infections and systematic diseases. Recent research on Macaque monkeys has shown that proteins extracted from the bacterium *P. gingivalis* can successfully immunize against periodontitis and prevent bone loss (16).

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