A UNIQUE BIOMEDICAL RESOURCE:
The Critical Contribution Made to Biomedicine Through Ethically Conducted Research with Chimpanzees

The chimpanzee *(Pan troglodytes):* Due to their evolutionary similarity to humans, chimpanzees have contributed to many areas of life-saving research. While a significant amount of work with chimps is behavioral in nature, the role that they have played in biomedical research has been significant, and has provided us with vaccines against hepatitis B and hepatitis A (*1*), infectious diseases that according to the Centers for Disease Control and Prevention (CDC) still infect as many as a million Americans every year, and annually cause more than 620,000 deaths worldwide. Chimpanzees remain an invaluable resource, and are unique because they are susceptible to many major health risks for humans, and therefore play a critical role in research on hepatitis C (*1*), malaria (*2*), and HIV (*3*). Chimpanzees are making important contributions towards stem cell research and the fight against cancer (*4, 5*). Chimpanzees are also the closest model for human cytomegalovirus (CMV) infection (*6*), which according to the CDC, is the most common congenital infection in the United States, and causes one child to become disabled every hour.

A chimpanzee that died in 2004 from heart failure, his cells preserved for future research, provided the genetic sample used to produce the genome sequence of a chimpanzee. Although they are 99 percent genetically identical to humans, studies of the tens of millions of differences between our DNA and theirs are shedding light on some of the Nation's greatest health threats.

A Wealth of Knowledge: NIH's Pub Med lists roughly 6,700 non-behavioral chimpanzee research publications produced since 1867. In the 150 years of recorded biomedical research with chimpanzees, more than 10% of the published research has been conducted in the last decade. This increasing trend can be correlated to the publication of the chimpanzee genome in 2005 (*7*). While many have asked what the new knowledge will mean to captive primates, it has been stated that our ability to care for wild populations could benefit from an increased understanding of great ape medicine (*8*). Current research trends make clear that our increased understanding of human and ape genomics and proteomics, technological advances in research techniques, and the contribution made from both comparative and biomedical research with chimpanzees has been and will continue to be invaluable for both human health and primate conservation. Chimpanzees have made a tremendous contribution to our understanding of evolution and biology. They are a unique biomedical resource that have pushed our bounds of understanding, and shaped the parameters of scientific ethics.

A Limited Biomedical Resource and a Long-Term Commitment: Today, research with chimpanzees continues to make critical contributions to research conducted in the U.S. through the CDC, FDA, and NIH. While the NIH's National Center for Research Resources (NCRR) acknowledges the continuing importance of chimpanzees to biomedical research, since their support of a breeding moratorium on chimpanzees in 1995 for financial reasons, their numbers have decreased. Although chimpanzees housed in the nation's primate research centers typically live for 30 to 45 years, unless the moratorium is lifted and policymakers voice support for this critical work, there may be no chimpanzees left for study in the US by 2037 (*9*). In the U.S., chimpanzees that contribute to biomedical research receive the best of veterinary care (*10, 11*), live a full life, and are not euthanized. The unprecedented human resources and financial commitment to chimpanzees housed at medical research facilities attest the fact that assuring the health and psychological well-being of chimpanzees for their entire lives is of the utmost importance.

Comparative Genomics & Cancer:

Although by DNA analysis they are 99% genetically identical to humans, studies of the literally tens of millions of differences between chimpanzee and human DNA are shedding light on some of the Nation's greatest health threats. Using both tissue and blood samples, researchers have carried out the largest study of the differences between human and chimpanzee genomes. Through comparative genomics, scientists have identified regions of DNA that have been duplicated or lost during the molecular evolution of the two lineages (*12*). Comparative genomic research has provided new evidence for a gene that has been associated with susceptibility to infection by HIV (*13*). Due to the low incidence of cancer in chimpanzees, comparative genomics is also shedding light on potential therapies for hereditary cancer in humans (*14, 15*).

Hepatitis:

Hepatitis is a major risk factor for liver cancer that affects more than 520 million people globally who suffer from chronic infection with either hepatitis B or C. According to the CDC, approximately 4.5 million of those people live in the United States. 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. Research to develop new therapies for hepatitis B,C, D, and E, as well as a vaccine for hepatitis C continues today (*16, 17*).

Human Immunodeficiency Virus (HIV):

Chimpanzees are poised to play a crucial role in the search for a vaccine against AIDS through the recent discovery of AIDS in wild chimpanzee populations (*18*) and the insight provided by comparative genomics (*3, 19*). According to the CDC, the estimated number of new HIV infections for the United States in 2006 was 56,300, or roughly 22.8 per 100,000 individuals. A substantial reduction in HIV incidence will require wider implementation of the effective interventions currently available and the development of interventions such as a vaccine (*20*), and monoclonal antibody therapies (*21, 22*).

Malaria:

Malaria is one of the most ubiquitous and severe public health problems. Malaria is a leading cause of death and disease in many developing countries, and according to the World Health Organization's (WHO) 2005 World Malaria Report, it is the leading cause of death in children under five years of age. Chimpanzees are vulnerable to infection by malaria and are an essential model in the research to develop a vaccine against this deadly infectious parasite (*2*).

Amyloid and Prion Diseases:

Chimpanzees are uniquely susceptible to amyloidosis (*23, 24*), diseases that include conditions such as Alzheimer's, which are caused by insoluble fibrous proteins. Chimpanzees are also susceptible to Transmissible Spongiform Encephalopathies (TSE's or prion diseases) such as "*Mad Cow" (BSE)*, Scrapie, and Creutzfeldt-Jakob disease. As a result, chimpanzees are one of the most relevant models of human prion disease (*25-27*). In 2001, chimpanzees played a crucial role in proving that infectious prions were not removed from surgical equipment via traditional sterilization methods (*28*).

Rotavirus, Norovirus, and Respiratory Syncytial Virus (RSV):

Chimpanzees are susceptible to many viruses that infect humans, and are therefore an important model for vaccine development. Chimpanzees can contract these viruses either in the wild or through contact with infected humans. Such viruses include common causes of gastrointestinal disease such as rotavirus and norovirus, as well as respiratory syncytial virus (RSV), which can cause life-threatening respiratory infections in infants, young children and the elderly.

siRNA, miRNA, and Humanized Monoclonal Antibody Therapies:

Perhaps the greatest value of the chimpanzee as an animal model in human health research is in safety and efficacy testing of these therapies. Recently a seemingly safe humanized monoclonal antibody therapy was tested in six human volunteers in the United Kingdom (UK); all six volunteers nearly died after they immediately became critically ill. This experimental therapy was tested in monkeys instead of chimpanzees and was thought to be safe. Unfortunately, in response to animal rights activists, the UK and many other countries have banned the use of great apes, including chimpanzees, as animal models for human health research (*29, 30*) and the research that would have halted this procedure was not conducted prior to human trials. Due to the similarity of their immune system to humans, if a chimpanzee animal model had been used this tragic outcome might have been averted.

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