Mice & Rats

The Essential Need for Animals in Medical Research

Introduction

Rodents play an invaluable role in biomedical research. Approximately 95 percent of all laboratory animals are mice and rats. Reducing reliance on higher-order species, rodents have become the animal model of choice for biomedical researchers because their physiology and genetic makeup closely resembles that of people. Despite certain differences between people and rodents, the similarities are strong enough to give researchers an enormously powerful and versatile mammalian system in which to investigate human disease.

The sequencing of rodent genomes has enabled researchers to recreate human diseases in rodents through genetic engineering. Researchers "knock in" or "knock out" disease-related traits in mice and rats, and new technology allows researchers to directly edit the DNA of the rodents[1]. Research with genetically modified mice and rats has led to significant new treatments, cures and therapies and continues to revolutionize science and medicine.

Cancer

Rodents have contributed to cancer research for more than a century[2]. Thanks in large part to the growing arsenal of rodent disease models available to researchers, much of our understanding of the development, prevention and curing of cancer comes from research in rats and mice.

Some of the most influential cancer drugs on the market trace their origins to discoveries in rodents. As an example, Herceptin, a hugely popular drug for breast cancer that improves long-term survival by nine percent[3], was developed with mice[4].

Rodent models brighten the future of cancer treatments and cures. Starting with research that showed a modified herpes virus could fight tumors in mice[5], the "oncolytic virus" concept developed into a successful clinical trial in melanoma patients in 2013[6]. In recent years, studies with mice and rats have highlighted a variety of exciting potential therapies for cancer, including tiny nanoparticles that deliver toxins to ovarian cancer cells[7], a vaccine to prevent breast cancer[8], and phototherapy that delivers light to destroy deep tumors[9].

Alzheimer's Disease

Rodents have greatly contributed to our understanding of Alzheimer's Disease (AD), and drugs derived from rodent research may help alleviate the tremendous economic strain of AD, which in the U.S. is projected to reach $1 trillion in yearly costs by 2050[10]. Rats are the most commonly studied experimental model of neurodegenerative diseases like AD[11]. Aricept, a common pharmaceutical treatment for AD that improves cognition in patients[12], was developed in rats[13], and Namenda, another common treatment, owes its approval for treating Alzheimer's in part to rat research into neurotoxicity[14].

Aricept and Namenda, like other currently available treatments, only treat AD symptoms. Drugs that instead seek to change the course of the disease are now in clinical trial, thanks to studies with rodents. Studies in "knockout" mice showed how the BACE enzyme is critical to the development of the amyloid plaques associated with AD[15], and now a bevy of drugs that inhibit the BACE enzyme are making their way through clinical trials[16]. Also developed with mice, new vaccines that enlist the immune system to remove amyloid plaques are currently in human trials[17].

Cardiovascular Disease

Rodents have become widely used as models of cardiovascular diseases such as atherosclerosis[18] and heart failure[19]. In one prominent example, research in a rat model of heart failure led to the widespread clinical use of angiotensin-converting enzyme (ACE) inhibitors in the aftermath of heart attacks, a practice that decreases mortality by as much as 19 percent over the four years following a heart attack[18]. In addition, after a new statin drug was shown in rats to block an enzyme associated with high cholesterol[20], it went on to become the widely popular cholesterol-lowering drug Crestor, which garnered 22.5 monthly prescriptions in 2014[23].

Rodent research is creating an exciting horizon for cardiovascular disease treatment. Recent research with rats and mice has alerted scientists to the possibility of using growth factors[21] and stem cells[22] to regenerate cardiac tissue after a heart attack. Mouse research has also highlighted a promising future treatment for atherosclerosis — a molecule that lowers cholesterol levels in the blood and dissolves artery-clogging plaques by mimicking the body's "good" cholesterol[23].

Diabetes

Much of our understanding of type 1 and 2 diabetes comes from rodent models[24]. For example, one mouse model helped point the medical world to the realization that environmental factors may strongly influence the development of type 1 diabetes[25].

Currently popular treatments for diabetes originated in studies with rodents. The blood sugar-lowering oral drug metformin, one of the most common treatments for type 2 diabetes, was developed with the help of rat models[26]. Lantus, a long-acting form of insulin that treats both types of diabetes and in 2014 generated 10.1 million monthly prescriptions[27], was first tested in rats and mice[28].

In the future, rodents may help cure diabetes. For type 1 diabetes, researchers can transform stem cells into insulin-producing pancreas cells, and when transplanted into diabetic mice, these cells cure high blood sugar[29]. For type 2 diabetes, a human growth factor protein has been found to reverse insulin insensitivity in mice[30].

Infectious diseases

From viruses to bacteria to protozoa, rodent models have helped researchers study and develop treatments for a wide range of infectious diseases.

In the development of antibiotics to fight against bacterial infection, rodents are essential partners. Penicillin, the watershed antibiotic that transformed the course of human medicine, was first tested in mice in 1940 before reaching WWII soldiers and the wider market[31]. Testing with rodents helped make available the modern antibiotics amoxicillin[32] and azithromycin[33], which together garnered a combined 101.5 million prescriptions in 2014 alone[34]. As medical research scrambles to address the growing problem of bacterial resistance to antibiotics, studies with rats helped bring more recent antibiotics like daptomycin[35] and tedizolid phosphate[36] to the treatment of drug-resistant gram-positive bacteria and staph infections, respectively, and research with mice helped select PA-824[37] as a candidate antibiotic to treat drug-resistant tuberculosis.

Once an unstoppable killer, HIV infection has become closer to a manageable condition, thanks to research with rodents and other animals. Research with rats[38] helped develop the antiretroviral drug cocktail that can successfully prevent the transmission of HIV from mother to child[39]. Research with mice with "humanized" immune systems helped lead to the first prophylactic treatment for HIV in 2012, Truvada[40]. These humanized mice are aiding researchers in the quest for the Holy Grail of HIV research, a safe and effective HIV vaccine[41].

Human medicine would not be where it is today without the incredible contributions of these small yet mighty animals.

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