RATS & MICE

The Essential Need for Animals in Medical Research

Introduction

Approximately 97 percent of all lab animals are mice and rats. Easily housed and bred, short lived (2-3 years), small, and relatively inexpensive, these rodents have become the animal model of choice for modern medical and scientific researchers. Because their physiology and genetic make-up closely resemble that of humans, rodents play an invaluable role in biomedical research. In the last decade, scientists discovered how to breed mice with genetic alterations that mimic human diseases. This capability has revolutionized medical research and dramatically increased the number of mice needed in medical science. The mouse genome is believed to contain essentially the same complement of genes found in the human genome, so studying how the genes work in mice is an effective way of discovering the role of a gene in human health and disease.

Man-made, genetically altered rodents

Transgenic and knockout rodents have been created with revolutionary new technology. While transgenic mice have had a foreign gene (a piece of DNA) artificially added to their genomes, knockout mice have had a specific gene "turned off" or made useless. A great deal of promising research relies on these genetically altered mice. Transgenic rats also have been used in medical studies and found to be better models than mice for studying certain human diseases. Genetically altered rodents have allowed scientists to observe what happens during the progression of Parkinson's disease, cancer, cystic fibrosis, heart disease, memory loss, muscular dystrophy, and spinal cord injuries. Recently, the mouse and rat genomes were sequenced. This achievement promises to significantly advance biomedicine.[1]

Naturally occurring immunodeficient mice

SCID (severe combined immune deficiency) mice and nude (or hairless) mice are born without thymus glands and lack functioning immune systems. These mice are very important models for studying both normal and malignant human tissue. They also are needed to develop and evaluate new drugs without risking human lives.[2]

Alzheimer's Disease

Scientists have evidence that a buildup of plaques containing amyloid protein deposits in the brain is a characteristic feature of Alzheimer's disease (AD), a disorder that affects patients' memories and personalities. Rats and transgenic mice bred to carry a gene that over expresses human amyloid protein have become indispensable for understanding and evaluating new drugs to prevent or delay the onset of AD. And recently, researchers have shown that vaccinating these mice with modified amyloid protein slowed the progression of the disorder. Patients are now being tested to see if the vaccine is well tolerated and can help overcome AD.[3]

Aging

Measuring physiologic changes over an entire life span would take many decades to complete in humans. However, such studies can be accomplished on "fast forward" in normal mice and rats. Research has shown that a reduced intake of calories in rodents markedly increases longevity, retards physiological deterioration, delays, and in some cases, prevents the incidence of age-associated diseases.[4]

Carcinogen Testing

Scientists are evaluating several lines of knockout mice to study the mechanisms of carcinogenesis. They propose that such animals might be needed for routine testing of chemicals for carcinogenic potential. The results can be obtained more rapidly with fewer animals, and the outcome can be used effectively in chemical and drug safety assessments.[5]

Cancer

During the past decade much of our knowledge of how environmental agents damage DNA and cause mutations that enhance cancer risk has come from studies with rats and mice. Scientists have produced

cancer resistant mice that lack the ability to produce cyclin D1, a protein found in abnormally high amounts in human breast cancers. They propose that cyclin D1 therapy might be highly selective in inhibiting the growth of human breast cancer cells.[6]

Cystic Fibrosis

Cystic fibrosis (CF) is a childhood disease characterized by chronic lung congestion and digestive problems. CF is incurable and patients rarely live to see the age of 30. Scientists now know that CF is caused by a small defect in the gene that manufactures CTRF, a protein that regulates the passage of salts and water in and out of cells. Studies with CTRF-deficient mice have shown that the disease results from a failure to clear certain bacteria from the lung, which leads to mucus retention and subsequent lung disease. These mice have become models for developing new approaches to correct the CF defect and cure the disease.[7]

Drug Addiction

Rats trained to self administer cocaine have high predictive value for human addiction because they share common triggers of relapse. In mapping the brains of adult rats that kicked the cocaine habit, researchers found that in relapse, the "high" from cocaine occurs in an area separate from where the brain retains cocaine-seeking behavior. This finding opens the possibility for developing new targets for anti-craving medication. [8]

Spinal Cord Injury

Scientists are using rats to study the mechanisms underlying long-term recovery of motor skills after spinal cord injury. They found that motor function is related to the number of intact axons, the part of the nerve cell that transmits signals to motor neurons. Recent studies have demonstrated that axonal sprouting or regeneration at the injury site correlates with functional recovery and can be enhanced by the application of certain growth factors to the spinal tract. Development of these approaches to neural repair may ultimately generate new strategies for treating human spinal cord injury.[9]

Heart Attack

New research has revealed that the heart muscle regenerates to some extent after a heart attack. A new strategy for treating this condition is being studied in transgenic mice. Researchers are experimenting with injecting stem cells (primitive bone marrow cells) into the periphery of the injured area to stimulate self-repair. The studies showed that the cells promoted structural and functional repair of the damaged tissue. [10]

References

1. Mouse Genome Sequencing Consortium *Nature* 420, 520-562 (2002). Rat Genome Sequencing Consortium *Nature*. Accepted for publication January 2004.

2. Bosma MJ, Carroll AM. 1991. The SCID mouse mutant: definition, characterization and potential uses. Ann Rev Immunol 9:323-350.

3. Schenk D et al. 2000. Immunization with amyloid-beta attenuates Alzheimer disease-like pathology in the PDAPP mouse. Nature 400:173-177.

4. Masoro EJ. 2000. Caloric restriction and aging: an update. Exp Gerontol 35:299-305.

5. Gulezian D et al. 2000. Use of transgenic animals for carcinogenicity testing: considerations and implications for risk assessment. Toxicologic Pathology 28 No. 3 482-499.

6. Yu Q et al. 2001. Specific protection against breast cancers by cyclin D1 ablation. Nature 411:1017-1021.

7. Stotland PK et al. 2000. Mouse models of chronic lung infection with pseudomonas aeruginosa: models for the study of cystic fibrosis. Pediatr Pulmonol 30:413-424.

8. Vorel SR et al. 2001. Relapse to cocaine-seeking after hippocampal theta burst stimulation. Science 292:1175-1178.

9. Benowitz LI et al. 1999. Inosine stimulates extensive axon collateral growth in the rat corticospinal tract after injury. Proc Natl Acad Sci USA 96:13486-13490.

10. Orlic C et al. 2001. Bone marrow cells regenerate infarcted myocardium. Nature 410:701-705.

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