University of California, San Diego

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CALIFORNIA SOCIETY FOR BIOMEDICAL RESEARCH

Super Scientists

HOW MICE ARE HELPING SCIENTISTS SOLVE THE MYSTERY OF DISEASE

Helping Scientists Solve the Mystery of Disease

CANCER. AIDS. ALZHEIMER'S, AND HEART DISEASE. THESE ARE SERIOUS MEDICAL CONDITIONS THAT ARE SURELY FAMILIAR TO YOU.

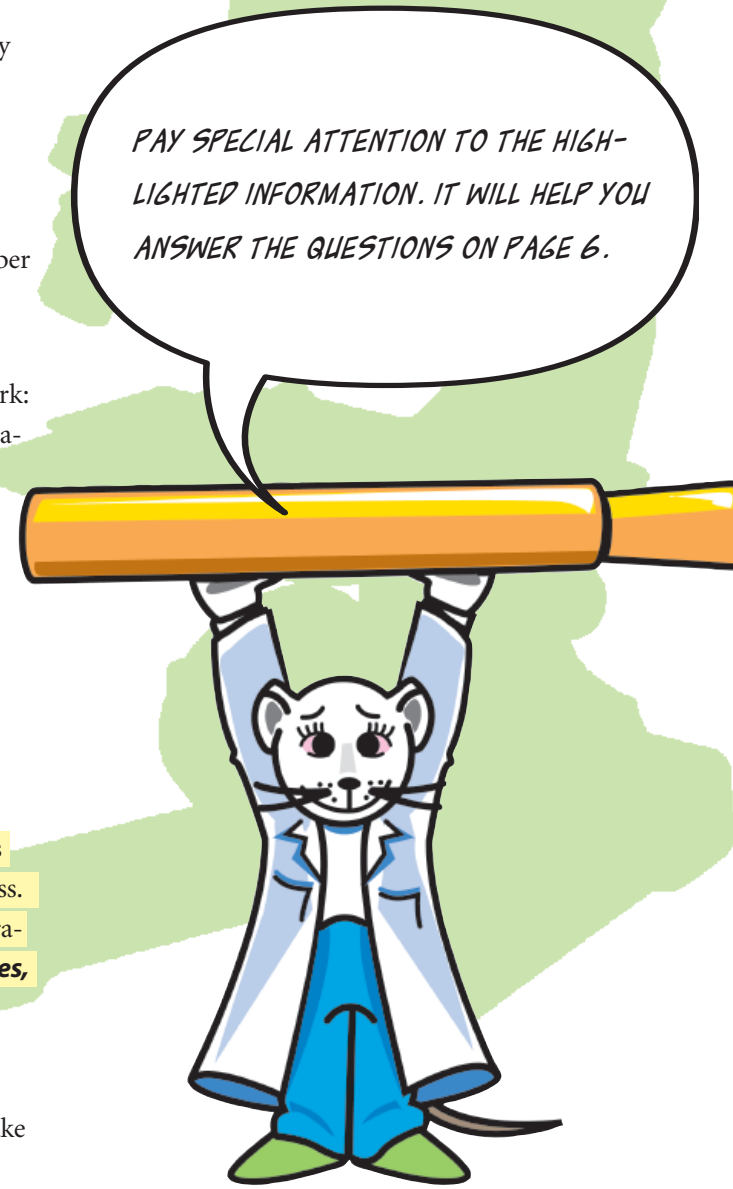
Maybe you have a friend or relative who actually has one of these diseases, or another condition just as serious. Did you know scientists are now working toward the time when such diseases may be prevented, or even cured?

In reaching this goal, scientists must first better understand the role that ***genetics*** and ***heredity*** play in human disease. For instance, scientists are trying to answer questions such as why one member of a family may get cancer and another may not.

To answer questions like these, researchers are using some unlikely "super scientists" in their work: laboratory mice. Despite their tiny size, these creatures pack a powerful punch in a relatively new field of study called ***transgenic research***. This science allows researchers to transfer "healthy" and "unhealthy" genes from one organism (or living thing) to these laboratory mice so that better treatments can be developed to prevent and cure sickness.

Through this research, scientists are breeding mice that develop human-like conditions—yes, mice that actually get human cancers, Alzheimer's disease, or show signs of asthma and other sickness. How is this possible? Scientists change these laboratory animals' genetic material in the ***chromosomes,*** an important part of the cell that carries hereditary messages. We hope to understand which of our many ***genes*** (the material in our body that contains all our inherited traits) go wrong to make us sick.

By creating "unhealthy" or defective genes in laboratory mice, scientists learn how "good" genes function. So, as you can see, these important animals help scientists discover new ways to predict, prevent, diagnose, and treat disease in humans.



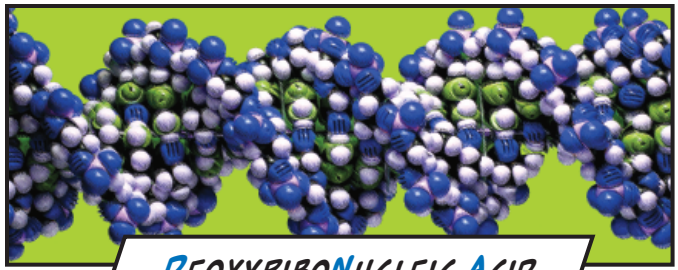
Hi Kids, Let's Talk About Genetics!

HELLO, SCIENCE STUDENTS. MY NAME IS DR. CAROL MACLEOD. I AM A SCIENTIST AT THE UNIVERSITY OF CALIFORNIA, SAN DIEGO. I AM A CANCER GENETICIST, WHICH MEANS I STUDY GENES IN CANCER AND HOW THEY SOMETIMES MAY BE INHERITED (PASSED DOWN FROM ONE FAMILY MEMBER TO THE NEXT) AND CAUSE DISEASE.

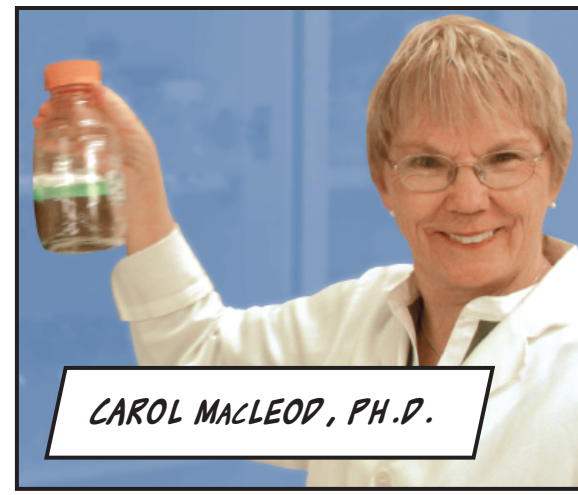
So that you may better understand my work and the important role our laboratory mice play, let's first talk a little about ***genetics***—the branch of biology that deals with the heredity and differences in various living things.

Just as genetics played a part in whether you were born with brown eyes or blue eyes and certain other characteristics that make us unique, genetics also is a key factor in determining whether we may be susceptible to certain diseases.

Your body contains about 60 trillion cells. Cells, as you may know, are the body's building blocks. Within the ***nucleus*** of each cell reside ***chromosomes***—essential genetic material that contains twisted, double strands of ***deoxyribonucleic acid*** known as ***DNA***, or the chemical containing the "secret code" information for our bodies and all other living things. (Did you know that you have 46 chromosomes—23 inherited from your mother and 23 from your father?)



DEOXYRIBONUCLEIC ACID



CAROL MACLEOD, PH.D.

Think of DNA as a twisted ladder where hundreds of thousands of genes are strung together in precise order. These units of DNA contain the code to give your cells the proteins they need to help keep you healthy and to sustain life. However, if a gene in the strand is missing, incomplete, damaged, or duplicated, it can cause disease.

This is very important when you realize that *each* of your cells contains about 100,000 genes, and if just a *single* one is abnormal or changed, it can increase your risk of becoming ill. Combine this with other external factors (such as a poor diet and whether you smoke) and it can increase your risk of illness even further.

This is where the laboratory mice come in. By using specially bred mice in genetic studies, scientists are learning the function of important genes. At the same time, other scientists are attempting to discover and "map" the location and exact order of each of the 100,000 human genes on the chromosomes, much as you might use a map to find a city located on a river. As you may have heard in class and in the news, this effort is known as the Human Genome Project.

The use of these laboratory mice in the discovery and mapping of human genes will help us to better understand gene function and to discover which parts of a gene contribute or do not contribute to causing disease. In this way, better treatments can be devised to prevent or cure illness.

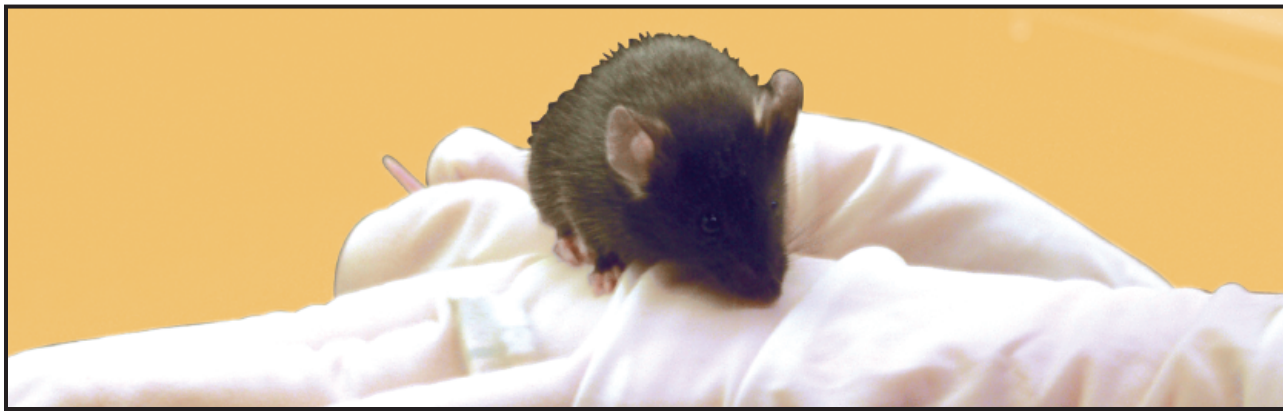
Why Use Mice?

DID YOU KNOW THAT 95 PERCENT OF ALL ANIMALS USED IN RESEARCH ARE RODENTS?

Mice are commonly used in transgenic research because their DNA structure is about 80 percent similar to that of humans. That's pretty close, isn't it?

Like humans, mice are also mammals and their bodies have the same organs that work in very similar ways. Of course mice are tiny compared to humans, but their biology is very similar.

Mice also make good research models because their life span is relatively long and their gestation (the time from pregnancy to giving birth) is short. Did you know that an average mouse lives two years—and four weeks after birth, female mice begin to reproduce? This allows scientists to study generations of mice for long periods. Mice are also great research models because their size makes them easy to take care of and house.



Transgenic Researchers are Like Detectives Solving a Mystery!

LET'S TALK A MINUTE ABOUT HOW SCIENTISTS CONDUCT TRANSGENIC RESEARCH

Scientists can determine from family studies and genetic testing if a particular gene seems to be causing or contributing to a particular disease.

Like detectives trying to solve a mystery, scientists must first test their ***hypothesis***, or hunch. This is begun by locating, or isolating, the suspected "bad" human gene in the laboratory. After some special tests, they inject fragments of DNA containing the suspected bad human gene into the nucleus of a one-celled mouse embryo, or egg.

Let me illustrate how difficult this procedure is. Once the DNA fragments are inside the mouse egg nucleus, there is only a 1 percent to 5 percent chance that the transferred gene will become integrated as part of the mouse chromosome in a useful way. We have found ways to determine exactly which cells have received the DNA fragments into their chromosomes. When the DNA is integrated, the transferred gene is then part of the animal's genetic structure, or ***genome***, and is transmitted generation after generation.

After injection, the mouse embryos are implanted in the uterus of an adult female mouse. After birth, the baby mice are checked to see if they carry the integrated gene (now called a "transgene" because it has been transferred). When these transgenic mice become adults they will be bred with non-transgenic mice of the same breed, so that half of the offspring will contain the transgene and half will not. This ensures that with each generation of mice born, there is always a "control" group with which to compare the transgenic mice.

If the transgenic mice develop certain signs or symptoms associated with the disease being studied, and if the control mice do not, then scientists have proven a relationship between the suspected transgene and the disease.

Another approach scientists are using is called ***gene "knockout" therapy***. Instead of transferring genes from one organism to another, "knockout" therapy involves the actual physical removal of a good gene from a living system and replacing that gene with a defective one. Through this approach, scientists hope to do experiments that will help us understand important details about the disease and, after that, to make more effective and specific treatments.

The Future of Genetic Research

OVER THE NEXT FEW YEARS, BE PREPARED TO HEAR AND LEARN MORE ABOUT HOW GENETIC SCIENCE METHODS ARE OPENING NEW DOORS OF UNDERSTANDING TO WHAT SCIENTISTS BELIEVE COULD BE AS MANY AS 4,000 INHERITED DISORDERS. AND BECAUSE OF THEIR SPECIAL QUALITIES, LABORATORY MICE WILL CONTINUE TO PLAY A HEROIC ROLE!

As advances in medicine continue, ethical questions about whether science is going "too far" in its study of genetics will be debated. This should challenge you to become more informed on the subject. Each of us will have to personally come to terms with questions like: "Is it right to correct a gene in an unborn child—a gene which may or may not develop into a disease sometime in the future?"

Such issues complicate, but do not detract from, the hope that genetic research offers. The purpose of this science is not to make you prettier or smarter, or make one group better than another. The purpose is to reduce suffering. This is our responsibility as scientists.

Careers in Human Genetics

HEY, READERS: CHECK OUT THESE EXCITING CAREERS IN HUMAN GENETICS, AND THE TRAINING REQUIRED.

Clinical Geneticist and/or Researcher: Treats patients using information learned from genetic research. Requires a medical degree from a medical school, and additional training in a specific medical specialty such as pediatrics or internal medicine, followed by special training in genetics.

Medical Geneticist and/or Researcher: Performs genetic research in laboratories to help doctors treat patients. Requires a Ph.D. degree in cell genetics, molecular genetics, population genetics, or another related area, followed by additional study in genetics.

Genetic Counselor: Counsels and advises patients and families who are involved in genetic research studies, especially those who may be at risk, of a variety of inherited conditions. Requires a master's of science degree from an official program in human genetics and genetic counseling.

Genetics Laboratory Research Assistant: Assists the medical geneticists and others in conducting genetic research studies. Requires a master's of science degree from an official program in genetics/biological science.

Genetics Laboratory Technician: Helps the genetic laboratory research assistant and others in genetic research studies. Requires a bachelor's of science degree in genetics, biological science, or a related area.

Vet Technician: Also known as a veterinary assistant. Assists the veterinarian with animal patient care, including lab tests, radiology, surgery, and pet owner education and counseling. Requires a two-year associate degree in veterinary technology.

Veterinarian: Doctors of veterinary medicine are medical professionals whose primary responsibility is to diagnose and treat diseases and other medical conditions affecting animals, and to protect people from diseases transmitted by animals. In genetic research, veterinarians play an important role in supervising the proper breeding, raising, and care of animals used in science so that scientists can better study diseases. Requires three to four years of college study in mathematics, chemistry, biology, and other pre-veterinary medical coursework, followed by four years of study at an approved veterinarian school. Additional study is also required after graduation.

QUIZ YOURSELF

How well did you understand the information in this booklet? Test yourself and see how "gene smart" you really are!

1. _____ PERCENT OF ALL ANIMALS USED IN RESEARCH ARE MICE.
2. WHAT IS GENETICS?
3. WHAT IS TRANSGENIC RESEARCH AND WHAT IMPORTANT QUESTIONS ARE SCIENTISTS HOPING TO ANSWER THROUGH IT?
4. IN WHAT WAYS ARE MICE "HEROES" IN TRANSGENIC RESEARCH?
5. YOUR BODY CONTAINS APPROXIMATELY _____ TRILLION CELLS AND _____ CHROMOSOMES.
6. EXPLAIN HOW A MOUSE CAN ACTUALLY GET CANCER, ALZHEIMER'S DISEASE, OR ASTHMA.
7. ANOTHER TERM FOR DEOXYRIBONUCLEIC ACID IS _____.
8. THERE ARE APPROXIMATELY _____ GENES IN THE HUMAN BODY.
9. A MOUSE'S DNA STRUCTURE IS ABOUT _____ PERCENT SIMILAR TO THAT OF HUMANS.
10. WHY IS TRANSGENIC RESEARCH SO DIFFICULT TO CONDUCT?
11. HOW DOES GENE "KNOCKOUT" TECHNOLOGY DIFFER FROM TRANSGENIC SCIENCE?
12. THE PRIMARY PURPOSE OF GENETIC RESEARCH IS NOT TO MAKE YOU SMARTER OR PRETTIER BUT TO _____ SUFFERING AND DISEASE.

Handy Definitions

Biomedical Research – Medical research based upon the principles of biology, biochemistry, and physical sciences in studying, diagnosing, and treating disease. Such research often involves the use of laboratory animals.

Cell – The basic structural and functional unit of life.

Chromosome – A rod-shaped structure, located in the cell nucleus that serves as the carrier of hereditary messages.

DNA (deoxyribonucleic acid) – A string of hundreds of thousands of genes situated in precise order within the cell that contains the "secret code" information for our bodies and all other living things. In addition, DNA gives cells the protein we need to keep healthy and to sustain life.

Embryo – A mammal in the early stages of development before birth.

Gene – A segment of DNA that controls a hereditary trait.

Gene "Knockout" Therapy – An area of genetic science involving the actual physical removal of a healthy, or "good," gene from a living system and replacing that gene with a defective, or "bad," gene in an attempt to help scientists better understand a particular disease or condition.

Hypothesis – A tentative explanation for an observation, phenomenon, or scientific problem that can be tested by further investigation.

Genetics – The branch of biology that deals with the study of genes.

Geneticist – A scientist who studies genes and their hereditary traits.

Genome – A genetic structure and its DNA components.

Gestation Period – The period of development in mammals involving the time span from pregnancy to giving birth.

Heredity – The transmission of traits from parents to their children or offspring.

Human Genome Project – A massive effort by scientists to discover and "map" the location and exact order of each of the 100,000 human genes in an attempt to better understand gene function and to discover which parts of a gene contribute (or do not contribute) to causing disease.

Life Science – The branch of science (such as biology and medicine) that deals with living organisms and life processes.

Nucleus – The control center of all cell activity.

Organism – Any living thing.

Traits – Characteristics (such as skin color and eye color) passed on from parents to their offspring.

Transgene – A gene that has been transferred to another organism in transgenic research.

Transgenic Research – A relatively new area of science which allows researchers to transfer "healthy" and "unhealthy" genes from one organism to another so that particular diseases can be better understood, diagnosed, treated, and eventually cured.

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Writer: Michael Dabney, UCSD

Editors: Marky Pitts, UCSD and Allison Chilcott, CSBR

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