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The Jackson Laboratory

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Founded in 1929 in Bar Harbor, Maine, The Jackson Laboratory is a not-for-profit, independent research institution dedicated to the study of mammalian genetics. With a 1996–1997 budget of $47.2 million, the Laboratory is composed of 36 major research groups and employs more than 830 people, including scientific, administrative, and animal resources staff. The mission of The Jackson Laboratory is threefold: (*1*) to conduct basic biomedical research to better understand genetic influences on human health; (*2*) to educate and train members of the scientific community; and (*3*) to enable worldwide biological research by providing genetic resources.

From its beginnings as one of the world's first centers for the study of cancer genetics, the Laboratory has expanded its scope to encompass a broad range of activities in mammalian genetics and biomedical research. Current areas of scientific investigation include cancer, developmental biology, aging, immunology, hematology, metabolic disease, neurobiology, sensory deficits, computational biology, and bioinformatics.

The Jackson Laboratory is one of eleven cancer centers designated by the National Cancer Institute to conduct basic cancer research. The Laboratory is a primary supplier of genetically defined laboratory mice to researchers worldwide and it serves as the national repository of mice with targeted and transgenic mutations for the study of human disease. It is also recognized as the international center for mouse genomic information.

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Historical Overview

The Jackson Laboratory was founded by Harvard-trained geneticist Clarence Cook Little. In 1924, during his tenure as president of the University of Maine, Dr. Little started a summer field course for the university's biology students amid the coastal splendor of Bar Harbor. He continued the popular course after joining the University of Michigan as president in 1925. Dr. Little left Michigan in 1929 to fulfill his dream of building a year-round genetics research institution in Bar Harbor. The new Laboratory was named for Roscoe B. Jackson, head of the Hudson Motorcar Co., a prominent summer visitor to Bar Harbor who helped fund the facility.

Dr. Little was a genetics pioneer who recognized that the study of hereditary characteristics in mice could help solve human health problems. Mice and humans suffer from many of the same diseases and have similar genes and gene locations. Knowledge of the location and function of mouse genes can be correlated with defective human genes that cause disease. By using mouse models that have been discovered as natural mutations or developed through advanced genetic engineering techniques, scientists can determine the functions of disease-causing genes and evaluate potential therapies and cures for human ailments such as cystic fibrosis, AIDS, epilepsy, diabetes, Huntingdon's disease, atherosclerosis, glaucoma, hypertension, and Down syndrome.

The first inbred strains of mice were developed by Dr. Little beginning in 1909. These genetically identical mice are a mainstay of mammalian genetics research, permitting many different scientists around the world to study the same biomedical problems by using identical strains of mice. Largely as a result of The Jackson

Laboratory's own research and its commitment to providing unique, quality resources to the community, the mouse has become the primary experimental system for mammalian genetics research.

World-class research and scientific achievements are hallmarks of the Laboratory. Over the years, many Jackson researchers have been recognized for outstanding contributions to science. One such discovery in the 1940s was the MHC (major histocompatibility complex), a critical set of genes that determines the ability of our immune systems to respond to foreign antigens such as infectious viruses. Dr. George Snell shared the 1980 Nobel Prize in Physiology or Medicine for this pioneering work, which led to successful organ and tissue transplantation in humans and increased understanding of immune diseases.

Other research milestones at The Jackson Laboratory include the first demonstrated link between viruses and cancer, with identification of the mouse mammary tumor virus (MMTV) transmitted in the milk of nursing mice; the first experimental animal model (*ob* mouse) for study of obesity-related diseases; the first use of bone marrow transplants to cure a blood disease; identification and cloning of the cpe^{fat} mutation in mice; discovery and cloning (with collaborators) of the tubby (*tub*) mutation; and location of the *ATHS* gene that predisposes a person to atherosclerosis.

Dr. Little was succeeded as director of The Jackson Laboratory by Dr. Earl L. Green (1956–1975). Dr. Richmond T. Prehn served as the next director (1976–1980), followed by Dr. Barbara H. Sanford (1981–1988). Dr. Kenneth Paigen became the current director in 1989.

Current Research Overview

Cancer

Characterizing the genetic aspects of cancers and tumor growth remains a research focus today. Integral to studying cancer is the complex field of immunology, or the study of the biological system responsible for fighting disease. Cancer studies at the Laboratory range from investigating basic immunological pathways and their connection with the disease to exploring specific models of cancer, including cervical, mammary, ovarian, liver, and prostate cancers as well as leukemia, and conducting AIDS research. Research projects to elucidate the genetic basis of tumorigenesis and metastasis are also underway.

Developmental Biology and Aging

Unraveling the blueprint for mammalian development from conception to death is the focus of several research groups. Fertilization, embryology, and aging are the three broad categories that this work falls into. Investigations range from developing culture conditions associated with measuring egg development and in vitro fertilization, to piecing together gene pathways in embryogenesis, to the study of senescence (aging) and the onset of disease associated with old age.

Immunology/Hematology

The immune system is perhaps one of the more dynamic and complex systems in mammals. Genetic pathways and environmental stimuli interact, triggering and maintaining a defense system to guard the health of an entire organism; this includes the surveillance against cancer. In conjunction with the immune system, hematopoiesis is an essential component to maintaining health. The genetic basis for both immune function and hematopoiesis can be studied using defined mouse models for disease.

Metabolic Diseases

Researchers at The Jackson Laboratory are investigating different aspects of metabolic disease. Several million people worldwide are affected by obesity, diabetes, atherosclerosis, gallstone formation, hypertension, and glaucoma. Although these diseases are treatable, they still take a toll on society and individuals in health care, emotional, and physical costs. Deciphering the genetic basis for these diseases is the focus for some members of the staff. Many genetic models exist for a number of these diseases that are similar to the disease states seen in humans. The utility of these models is greatly enhanced by the current availability of transgenic and gene-targeting technologies.

Neurobiology and Sensory Deficits

It is estimated that 20,000 genes are specifically expressed in the mammalian nervous system. Their interactions and pathways are phenomenally complex, ranging from brain development to daily central nervous system function to con-

tributing to psychiatric states and behavior. Research at the Laboratory involves discovering gene mutations that can cause debilitating central nervous system diseases. Understanding the genetic basis for epilepsy and many sensory disorders as well as elucidating the function of specific cell types in the brain are foci for Jackson Laboratory investigators.

Education

The Jackson Laboratory regularly sponsors symposiums and conferences to provide a forum for the exchange of ideas and scientific findings. For 38 years, the internationally recognized Short Course in Medical and Experimental Mammalian Genetics, co-sponsored with Johns Hopkins University, has attracted biomedical investigators, clinicians, advanced graduate students, and teachers from around the world. This two-week course is a comprehensive survey of genetics as it relates to health and disease and has been attended by most of the world's leading geneticists.

In addition to the Short Course in Medical and Experimental Mammalian Genetics, other courses offered in 1998 include Cryopreservation of Mouse Embryos; Biotechnology: Products, Policy, and the Public (Third World Issues); Experimental Genetics of the Laboratory Mouse; Rodent Models in Modern Risk Assessment; Genetic Approaches in Complex Heart, Lung, and Blood Diseases; Cryopreservation I: Embryo and Gamete Collection, In Vitro Fertilization, Embryo Transfer; and Cryopreservation II: Freezing, Thawing, and Storage of Mouse Germplasm.

Academic-year programs for undergraduate, graduate, and postdoctoral students are also offered by the Laboratory. These programs permit young investigators to develop skills in research methodology and interpretation and often result in new ideas that benefit the Laboratory's own research programs.

The Laboratory's well-known 10-week Summer Student program provides qualified high school and college students an opportunity to conduct a research project, including proposal, implementation, and data analysis, under the guidance of a sponsoring staff scientist. Two alumni of the program, Drs. David Baltimore and Howard Temin, were recognized as Nobel Laureates in Physiology or Medicine in 1975.

Animal Resources

Each year, the Laboratory supplies approximately 1.5 million JAX mice from an inventory of more than 2,300 different stocks and strains to universities, medical schools, and research laboratories worldwide. Rigorous quality controls ensure the standardization, health, and genetic purity required for scientific research. The Laboratory operates the world's largest frozen mouse embryo repository, which preserves important stocks and strains of mice for use in future research.

The Mouse Mutant Resource (MMR) is the primary repository at the Laboratory of strains and stocks carrying spontaneous mutant genes. The MMR performs two vital functions: *(1)* characterization of new spontaneous mutations in mice that occur within the large breeding colonies, and *(2)* maintenance and distribution of established mutant stocks. Once characterized and described in publication, new mutants are made available to the scientific community.

The Induced Mutant Resource (IMR) was established in 1992 in response to concerns from the scientific community regarding the cost, health, and free distribution of genetically engineered mouse strains developed in research programs worldwide. The IMR serves as the national clearinghouse for the collection and distribution of such genetically engineered mice. The function of the IMR is to *(1)* select biomedically important stocks of transgenic, chemically induced, and targeted genetic models, *(2)* import these stocks into the Laboratory by standard procedures that rid them of any pathogens they might carry, *(3)* cryopreserve embryos from these stocks, *(4)* backcross the mutation onto an inbred strain if necessary to ensure genetic integrity, and *(5)* distribute them to the scientific community.

The Mouse DNA Resource extracts, purifies, preserves, and distributes high-quality DNA from JAX mice, providing molecular biologists with a ready source of DNA at any time.

Bioinformatics

The Jackson Laboratory has expanded its research base over the past five years, with Bioinformatics and Computational Biology being an integral part of that growth. Bioinformatics is the application of computers and databases to help store, retrieve, and analyze biological informa-

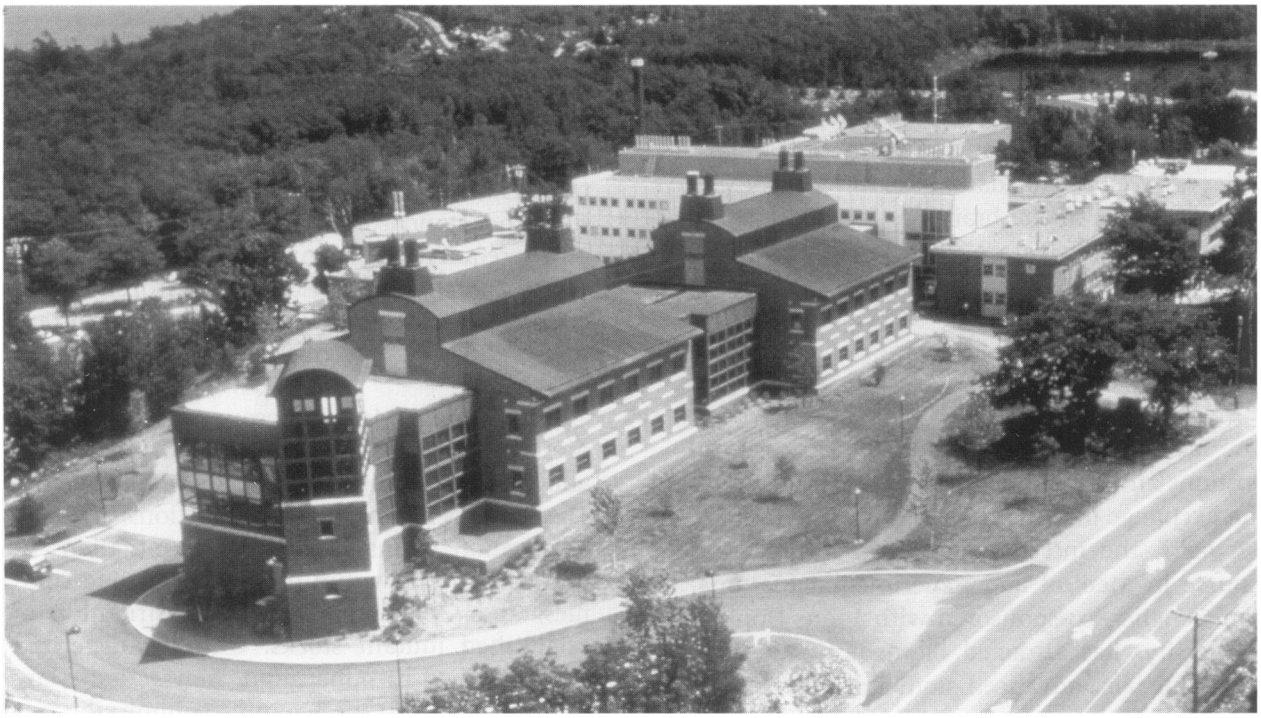

Fig. 1. The Jackson Laboratory.

tion, whereas computational biology refers to the development of software tools that address specific biological questions.

Contributions from The Jackson Laboratory to the field of Bioinformatics include two award-winning databases: The Encyclopedia of the Mouse Genome, which was a finalist for the 1992 Computerworld Smithsonian Institution award for innovation in information technology; and the Mouse Genome Database (MGD), which was nominated for the 1995 Computerworld Smithsonian award. In addition, one of the first gene expression databases, the Gene Expression Database for Mouse Development (GXD), will allow researchers to obtain information about gene expression patterns.

The Mouse Genome Database (MGD) provides the worldwide scientific community with a continuously updated resource for genomic and phenotypic data. Researchers using MGD, generally via the World Wide Web, can view primary, as well as analyzed and integrated, data in tabular or graphical formats. Software for analysis and display includes map tools to generate genetic, cytogenetic, and physical maps of the mouse genome with options for displaying mammalian gene homology information. Links to other on-line databases such as GDB, OMIM, and DNA sequence databases aid in analyzing mouse data in the broader biological context. Plans include the addition of a mouse tumor biology component.