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Mice as the Ribbon--History of Jackson Lab and animal model in Maine's Biology History

## Introduction

The history of biology in Maine is vibrant, particularly in the molecular biology and genetics area, thanks to the contribution of Jackson Lab, one of the most renowned biological science research institutions in the US. In 1972, Science magazine even called the Jackson Lab a "Mecca to anyone tuned into mammalian genetics (Rader 253)." To gain a deeper understanding of the history of biology, especially the research related to mice models at Jackson Lab in Maine, I will examine the general historical context of genetics advancement, Jackson Lab's initial elements and developments, its collaboration with Colby College since 1947, and some of the lab's recent findings and activities in the state. Eventually, the paper would provide a comprehensive picture of the history of biology, particularly mice models and related biology research in Maine.

## The Historical Background and the Beginning

Since the mid-19th century, evolution, natural selection, and genetics became general topics for biologists. Specifically, the rediscovery of the papers of Gregor Mendel served as the fundamental rules of genetic inheritance in Pea plants (Jackson Lab). From this point, the Chromosomal Theory of Inheritance solidifies. As chromosomes became the essential elements of inheritance, many researchers emphasized genetics research, and their passion is built upon the beginning of mice models' incubation and usage. In 1900, the Granby mice, which are breeding "fancy mice" by a retired schoolteacher Abbie Lathrop at her farm in Granby, Massachusetts,

became important in research, as it supports the growth in genetics research, specifically the genetic inheritance (Jackson Lab). Shortly after that, Coat Color genetics by W. E. Castle was proposed in 1903. In 1908, W. E. Castle opens Harvard's Bussey Institution, where many early mouse geneticists get their start (Jackson Lab). With systemic learning in mouse genetics, researchers became more comprehensive in understanding mice genomes, setting the foundation for the explosive advancement in humans' understanding of genetics and, eventually, clinical applications. Specifically, "the legacy of the inbred mouse as a 'model organism' today draws momentum from the choices made by Little and other early twentieth-century geneticists" (Rader 252). As one of these early mouse geneticists, Clarence Cook Little honed his knowledge and skills in mice inbreeding and corresponding genetic manipulations. For instance, Clarence C. Little inbred mice to eliminate variation, developed the first inbred strain, and designated DBA for dilute, brown, and non-agouti (Jackson Lab).

Until the 1920s, the usage of mice as a fundamental research model naturally elicited the establishment of an unofficial rule about research that used animal models: "albino rats, certain apes, and the guinea pig would be the paradigmatic, archetypal lab animals. In particular, specially bred lab rats were de rigueur, the obvious choice (Lemov36)." With such a fast-paced development in mice models and biological research in genetics, Jackson Lab was established to offer models and solutions to questions that have answers encoded in the genes of human beings. On May 4, 1929, Clarence Cook Little launched the lab with eight employees and $50,000 in support from benefactors and lands from family friend George B. Dorr (Peterson). Although the resources at the beginning were limited, the members of Jackson Lab contributed their passion to the development of mice incubation, cancer research, and genomics studies over decades.

**Mice Models and Research at JAX**

Since its establishment in 1929, Jackson Lab had developed and expanded its concentration from mice model inbreeding to new biological research areas like genomic medicine and cancer research, reflecting the lab's continuous efforts and involvement in the history and development of biology.

The research and incubation on mice models were essential elements for Jackson Lab since its establishment. The director and founder of Jackson Lab, Clarence C. Little, inbred mice since his early years as a student at Harvard University. The scientific area embraced his mice model as it provided a way for biologists to reduce the complexity in genetics, thus focusing on one genetic trait like the coat color and cancer susceptibility (Peterson). Shortly after Jackson Lab's establishment, Little led the faculties to focus on the sale of mice as the essential animal model for biology research in the US. According to Rader, bacteriologists and medical researchers in the late 1920s used mice in different experiments, ranging from research "on the immune system response, comparative physiology of blood pressure, epilepsy, and deafness to clinical pregnancy tests (131)." Noticing the great demand in mice as biological research models, Clarence C. Little developed a catalog of the features of the animals that he determined universally most helpful, and in 1933, he provided a primitive sales listing for all the inbred strains of mice (Rader). From this moment, Jackson Lab improves and advances step by step in the mice model incubation. In fact, the expanded efforts to sell Jackson Lab mice bring positive feedback and influence on Jackson Lab's reputation and resources, providing opportunities for more research at Jackson Lab, including further modification in mice models (Rader).

As time went by, the mice models also modified and diversified thanks to Jackson Lab staff members' significant contribution. Specifically, increasing genetic variation among mouse

populations is a new focus and aim for Jackson Lab staff. For example, in 2004, Jackson Lab Professor Gary Churchill, Elissa Chesler, and other leading lab mouse experts devised the "Collaborative Cross," a mouse population with eight different founder strains, including standard inbred strains and wild type strains (Peterson). These groundbreaking successes from Jackson Lab had helped the research in nature, treatment, and even the cure for cancer among humans. Thus, Jackson Lab is part of the history of mice modeling in biology over decades.

Besides the research in mice models, Jackson Lab's efforts and contributions in another area of biology with the application of mice models in experiments are also crucial for the history of biology. First, transplantation has always been a concentration of research since 1937. Initially, Peter Gorer's mouse studies in 1937 suggested that transplant rejection is primarily governed by the H2 genetic locus, later described as the major histocompatibility complex (a key component of immunity), marking the beginning of the biological research in this vital immunology concept (Jackson Lab). Then, from 1940 to 1950, William Russell conducted the first successful transplantations of ovaries between female mice (Jackson Lab). In the next few years, Elizabeth Russell pioneered the use of bone marrow transplantation to cure a blood disorder in a mouse (Jackson Lab). Finally, in the early 2000s, Jackson Lab professors participated in the research in which scientists successfully transplanted human immune system cells into the SCID (severe combined immune deficiency) mouse (Jackson Lab). At first, the success of transplantation among mice seems to be not significant. However, since mice's genomes are close to humans, and we understand and research their genomes thoroughly, these experiments on mice potentially shed light on similar treatments for human patients with the same disease. Consequently, Jackson Lab facilitated the evolution of biology and research, leading to medical applications for saving lives.

**The Community Engagement in Maine**

As one of the famous biology research-focused labs, Jackson Lab is not an isolated island in Maine. Instead, community engagement in terms of the biology research in Maine is frequent between Jackson Lab and other institutions, thanks to the historical advantages conferred by politics and the public's attitude.

The social and political circumstances' changes altered and propelled the research in genetics. World War II mobilized scientific researchers...into a new relationship with the federal government, and Americans more broadly into a new relationship with science (Rader). The reason for the tremendous support from the federal government since World War II was the opportunity to reveal the power of science in front of people. The atomic bomb was said to have won the war, and the Manhattan Project… was held up as an example of what science could do for the country if given enough resources (Rader). From 1940 to 1950, the public concern about radiation began to grow, spurred on by media reports on the sufferings of Japanese bomb survivors, which led to emphasis and support on radiation-related biological research. Subsequently, the beneficial relationship between federal cancer policy and JAX inbred mice got a dramatic boost when the American Cancer Society pressured the federal government directly to better coordinate NCI cancer research labs and cancer treatment clinics (Rader). Simultaneously, congress allotted nearly seventy million dollars over the period from 1956 to 1958 (Rader). Thus, the research of life to decode the mysteries took advantage of the financial and political "grace period" for biology and other science subjects. Under such circumstances, the benefits of the support of biology research reached Maine, notably Jackson Lab and Colby College, and these great opportunities led to continuous community engagement of Jackson Lab since then.

The collaboration between Jackson Lab and Colby College regarding cancer research in the late 1940s reveals Jackson Lab's active engagement in community work. The News about the cancer research support for Colby College is striking evidence. The image records the article from *Waterville Morning Sentinel* on May 6, 1948, archived at Colby Special Collection. It described a generous grant for cancer research from the American Cancer Society, including Jackson Lab and Colby College Biology and Chemistry department's participation in future cancer research. In the news report, Clarence C. Little expressed the positive provision for rehabilitation of the mice supply with the generous grant from the American Cancer Society. The successful rebuild of Jackson Laboratory from the fire in 1947 potentially allowed the close collaboration between Jackson Lab and Colby's Biology Department in the next few years. Also, according to the News, William Holt, the president of the Maine Cancer Society, "presented the $5000 grant to Colby College," which would be used for cancer research that was hoped to "lead to the discovery of a simple systemic test to determine either the present or absence of certain types of cancer." Moreover, according to the News, Julius Gottlieb would collaborate with Colby's Chemistry and Biology Department, suggesting the profound connection between Colby and Maine scientists. This news report marks the beginning of the cancer research that Colby's biology department would be involved in, reflecting the crucial roles of both Colby College and the Jackson Lab in Maine's history of biology. Both Jackson Lab and Colby College took advantage of the friendly political and social environment for biology research.

The summary of the Activities of Colby Cancer Project reflects the continuation of the future cancer research that includes efforts from Colby and Jackson Lab. Both Colby's Biology department faculty and students and the Jackson Lab actively engaged in cancer research, which uses mice as the essential animal model. Such a fact was supported by the document "The

Summary of the Activities of Colby Cancer Project." Specifically, the method that "2 cc of the residue concentrate was injected intraperitoneally in white rats weighing not less than 90gms or more than 110 grams (Bowers)" was applied in the research to examine the efficacy and feasibility of the newly proposed test theory for cancer. Also, this Cancer Project was closely related to the Clinical collected malignant urine of cancer patients in Maine's hospitals, showing the clinical significance of the research that Colby's biology department faculties and students were involved in. From this perspective, Colby and Jackson Lab were profoundly related to the development of biology at the state level in history. Besides, this report is in the standard format of the scientific report. It includes the detailed introduction, method, results, and discussion sections, presenting comprehensive information related to the one-year-long research. Colby College faculties and students concluded that "there had been no significant trend manifest (Bowers)," while suggesting possible changes and improvements in the future. Consequently, it shed light on future work with modifications of the methods and procedures on cancer research in Maine, which is beneficial to the biology advancement in the research arena. These collaborations with JAX and Maine scientists and doctors were extraordinary support for Colby's advancement in Biology research. Simultaneously, the collaboration serves as an excellent example of Jackson Lab's long-term community engagement regarding the development of biology research and mice model applications and advancement.

The connection and partnership between Jackson Lab and Colby College regarding biology research remain close and tight in recent years. According to the article "World-Class Research: Biomedical Science Beyond Experimentation," the Jackson Lab offers precious working opportunities for Colby College students with accomplished professors to immerse themselves in the biomedical research setting. Specifically, "the connections to … the Jackson Laboratory exist

alongside Colby's partnership offers a semester-in-residence program for Colby students (Colby Magazine)." Jackson Lab now has such a strong bond with Colby College regarding the biological research that involves the active participation of Colby College students, and such a scenario suggests the scientific community that Jackson Lab engages in at the state level. Such a continuation of the close collaboration between Jackson Lab and Colby College reflects the lab's active engagement in the collective community progress in biology research since early ages.

Besides the intimacy between Jackson Lab and Colby College, Jackson Lab also actively engaged in research with other scientists, leading to the diversified and fruitful outcome of genetics investigations using mice models bred at Jackson Lab. For instance, obesity and genetics were explored by Douglas Coleman from 1960 to 1973 (Jackson Lab). Coleman initiated a series of landmark experiments and postulated in 1973 that the ob mouse has a genetic defect in its 'satiety factor' and that the db mouse has a genetic defect in its 'satiety center.' Such a finding led to the successful cloning of the genes behind the ob and db defects, shedding light on the relationship between obesity and genetic inheritance. Later in 2002, the laboratories of Drs. Jürgen Naggert and Patsy Nishina announced the first human gene, a mutation in the gene ALMS1, which causes Alström syndrome, discovered at JAX (Jackson Lab). This discovery was said to open new pathways for understanding common human conditions, including obesity and diabetes potentially. Another development in research since the early 21st century is genetics. JAX Associate Professors Kevin Mills, Ph.D., and Joel Graber, Ph.D., discovered telltale variations in mRNA processing that correspond to cancer in 2010 using mice models (Jackson Lab). Their experiment showed that they could distinguish among similar tumor subtypes with at least 74 percent accuracy, a dramatic increase over current molecular cancer diagnostics. They also identified a molecule that prevents repair of some cancer cells, providing a potential new "genetic chemotherapy" alternative

to cancer treatment. A JAX research team led by Professor Lenny Shultz, Ph.D., reported that the protein iRhom2 could be a potential therapeutic target in 2014. By introducing mutations in Rhbdf2, the gene that encodes the iRhom2 protein, the researchers extend "the protein's duration and wound-healing power (Jackson Lab)." Thus, Jackson Lab, with strong connections to others in the communities at the state level, continues to grow and be involved in biology research at an unexpectedly high rate.

Besides the strong bond between Jackson Lab and other institutions for scientific research, Jackson Lab also actively participates in community work. For example, in recent years, Jackson Lab has offered regular, on-site training to employees like Confined Space Rescue Training, Laboratory Safety Training, and others to many organizations like MDI hospital, Acadia National Park, the Bar Harbor Fire Department, and more (Jackson Lab). Similarly, Jackson Lab co-sponsors and co-organizes annually for the Maine State Science Fair, which draws approximately 500 high school students from across the state to compete for a college tuition scholarship (Jackson Lab). Jackson Lab's activities that facilitate the development of biology are not limited to the mice incubation and collaboration focused on advanced scientific research. Instead, Jackson Lab persistently supports the education and development of new generations to offer more access to biology. From this aspect, the bond between Jackson Lab and the community in Maine is solidified in various ways. So naturally, Biology in Maine also grows and advances with such an optimal condition.

## Conclusion

Jackson Lab is a unique lens that provides us with new understandings about the development of biology, especially genetics and cancer research conducted in Maine. Countless contributions and fruitful outcomes occurred with the collaboration of many scientists and students since the

early 20th century. By reviewing the history and development of Jackson Lab in Maine, we understand the close connection between Jackson Lab and Maine's history of biology. This part of history reflects not only the importance of collaboration in biology for discoveries and continuing explorations but also the bright future of the biology development in Maine, thanks to the continuous collaboration and contribution from Jackson Lab. With the collective effort from different institutions, biology would continue to be nurtured in Maine's friendly environment. Starting with mice, Jackson Lab has created its unique bond with the community in Maine, offering its power and passion to the growth in biology.

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