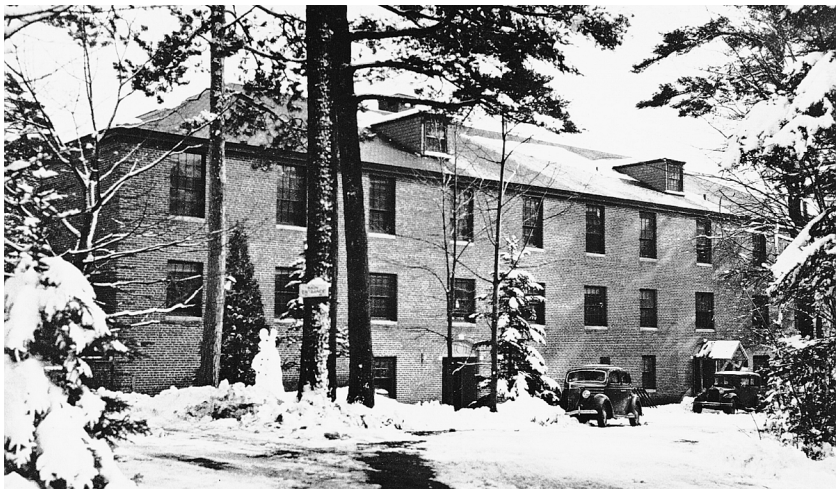
INTRODUCTION

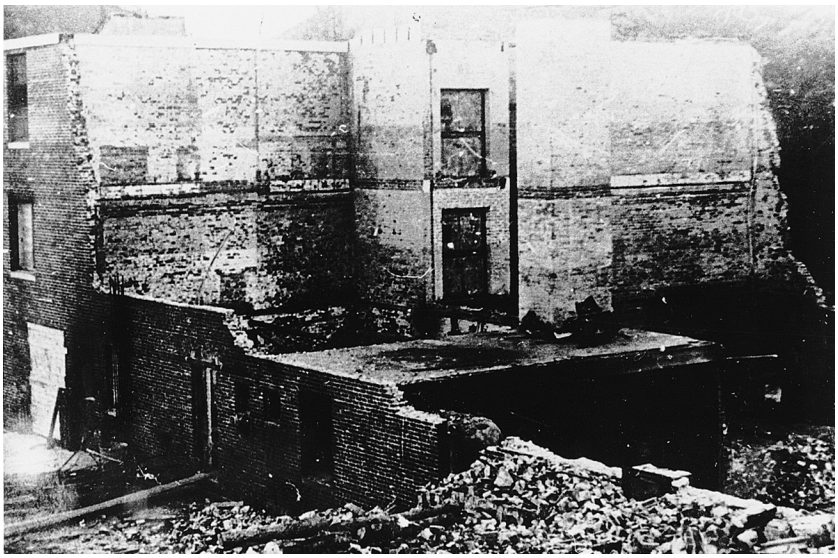
WHY MICE?

On October 23, 1947, fourteen people and tens of thousands of laboratory mice perished when the sleepy resort community of Bar Harbor, Maine, burned to the ground. A forty-mile wind-borne fire front triggered early evacuation of most of the town's estimated 4,300 human residents. Some escaped by car or bus, and thousands more rushed to the docks to await rescue; the scene, a Coast Guard official told the *New York Times*, "was reminiscent of Dunkirk." Many loyal caretakers of the island's nearly three hundred palatial estates stayed behind to fight the flames "with nothing but brooms." Elizabeth Russell, a scientist at the Jackson Laboratory, Bar Harbor's nearly twenty-year-old institution for research in mammalian genetics and cancer, remembered seeing a small plume of smoke on October 14, while at a staff meeting at nearby Hamilton Station, and marveled at how the "tiny fire had continued to grow." She and the rest of the staff quickly escaped the premises and were spared injury, but their experimental organisms fared less well. The fire completely destroyed the original lab building, and two new "mouse houses"—the second of which was under construction at the time—were seriously damaged. Except for the few hundred mice readied for shipment to researchers in a corner isolation room, all ninety thousand resident rodents (housed primarily in wooden mouse boxes) died in the blaze. When the embers cooled, those who first arrived on the scene remember two things: the strange and unforgettable smell of burnt mice, and the comment that the lab's founder, geneticist Clar-



I.1. Jackson Memorial Laboratory, c. winter 1935 [Source Credit: Jackson Laboratory Archives].

I.2. National Guardsman in front of the Jackson Memorial Laboratory, the day after the October 1947 "great Bar Harbor fire." [Source Credit: Jackson Laboratory Archives].



I.3. View of mouse rooms burned by fire, Jackson Memorial Laboratory, October 1947 [Source Credit: Jackson Laboratory Archives].

I.4. C. C. Little meets the press and surveys the damage, October 24, 1947 [Source Credit: Jackson Laboratory Archives].

ence Cook Little, made upon surveying the damage: "Now we can see the water"[1] (fig I.1–I.4).

The next day, as Maine's governor scrambled for federal disaster relief money to rebuild America's "Vacationland,"[2] Little received multiple unsolicited offers of aid to re-establish the "JAX" mice (as they had come to be known, from an abbreviation of the lab's cable address). The Rockefeller Institute for Medical Research and the Carnegie Institute both pledged facilities for maintaining the surviving mice, and before they knew the full extent of the damages, the boards of the American Cancer Society and the National Institute of Health (NIH) held special meetings where they decided to offer Little a replacement building for the continued production of mice in Bar Harbor. But perhaps most remarkably, individual geneticists and medical researchers who had previously received stocks of JAX mice began sending back breeding pairs of those same stocks to Bar Harbor. Little told the Rockefeller Foundation's Warren Weaver that there was "hardly a genetics or cancer research institute east of the Mississippi" that didn't respond to his lab's crisis. He analogized the animals' return to a biblical miracle: "The bread which we cast upon the waters several years ago, is now returning to us."[3] By contrast, Little claims to have received only one angry letter from a local "anti-vivisec-

[1] On the Bar Harbor evacuation, see Frank L. Kluckhohn, "18 Dead, Damage $25,000,000, as Forest Fires Sweep on in Wide New England Area," *New York Times*, 25 October 1947, A1+, and "Much of Bar Harbor Razed as 4,300 Flee Forest Fire; Whole Maine Towns Gone," *New York Times*, 24 October 1947, A1+. For a comprehensive list of fire-related media articles, see Jackson Laboratory Association folder, Box 735, and Fire folder (with sample articles), Box 730, both CCL-UMO. On the lab's losses, see 19th Annual Report of the Jackson Laboratory, 1947–48 (JLA-BH). On postfire memories, see interviews with George Snell (June 1995) and Joan Staats (June 1993), both JLOH-KR. Quotes from Elizabeth Russell are from her published recollection, "Mouse Phoenix Rose from Ashes," in *Perspectives on Genetics Anecdotal, Historical, and Critical Commentaries, 1987-1998*, ed. James F. Crow and William F. Dove (Madison: University of Wisconsin Press, 2000), pp. 29–30 (originally published in *Genetics*, October 1987). Russell remembered Little's postfire statement slightly differently: "Now we can see the sea."

[2] See George Lewis, "The Maine That Never Was: The Construction of Popular Myth in Regional Culture," *Journal of American Culture* 16, 2 (Summer 1993): 91–99.

[3] Emergency telegrams are contained in Box 735, CCL-UMO. For some sample scientific responses to the JAX Lab fire, see WW to K. Compton, 3 October 1947; WW to RBF, 7 November 1947; both RF Archives, RG 1.2, 200A, Box 134, Folder 1191, RAC-NY; "RBJ Lab," RF Trustees Bulletin, November 1947. See also CCL to WW, 21 and 28 November 1947, all RF Archives, RG 1.1, 200D, Box 144, Folder 1777, RAC-NY. For a specific example of a "mouse return," see CCL to Muller, 3 November 1947; Muller to CCL, 7 November 1947, CCL to Muller, 17 November 1947: all in the H. J. Muller Ms., Manuscripts Department, Lilly Library, Indiana University-Bloomington. For biblical rhetoric, see 1948 JAX Annual Report (public version) and a 1952 film produced by JAX Lab on the subject, R_x Mouse, c. 1950–52, both in JLA-BH.

tionist women's club," which expressed regret "that Dr. Little and his fellow scientists had not been burned up in the blaze instead of the mice."[4]

By 1949, national fundraising drives combined with additional governmental support to ensure that Jackson Laboratory would rise from its ashes. That year in a foundation endorsement letter, the lab's Board of Trustees noted that the institution had been completely rebuilt and had reclaimed its status as the "Bureau of Biological and Medical Standards." During the fall of 1953, Little felt so confident about the lab's future that he contacted his lawyer about his ultimate wish: to link the success of the JAX mouse to another popular mouse who had also weathered the Depression era. He wrote:

> I was very much interested in the article in *Life* on the 25th Anniversary of Mickey Mouse. . . . 1954 is also the 25th Anniversary of the Jackson Laboratory, that in a somewhat similar, but less sensational, way has done for the mouse in science what Disney has done for it in amusement. The possibility of arousing Disney's interest in doing something of a philanthropic nature along the line of a factual, or partly factual film, to tell the story of the mouse (which might easily be a brother or other relative of Mickey) has been in [our] minds . . . for some years.

Little did eventually correspond with Disney, but apparently nothing ever came of his idea. He later told a friend the moral he drew from this interaction, as well as from public responses to the 1947 fire: "In these days, when support of basic research by the American public is its chief and constantly growing hope, efforts of this kind, which might seem through Victorian eyes to be undignified, are not really as shallow and superficial as they may seem."[5]

[4] On the Bar Harbor antivivisectionists, see Arthur Bartlett, "The Big Mouse Man of Cancer Research," *Coronet* 26 (August 1949): 161–62. The letter's author also objected to the well-publicized JAX experiments on rabbits, which aimed at trying to create "good" and "bad-tempered" strains through genetic inbreeding. But Little refused even to respond to this argument of individual animal integrity and replied: "Dear Madame: The members of your club seem much more bad-tempered than the rabbit." Bartlett himself concluded that Little's mouse work represented the only noble social ethic: "scientific progress in service to humanity." For an overview of antivivisection in the United States circa 1900 and beyond, see Mary L. Westermann-Cicio, "Of Mice and Medical Men: The Medical Profession's Response to the Vivisection Controversy in Turn of the Century America," Ph.D. dissertation, State University of New York, 2001; Susan E. Lederer, *Subjected to Science: Human Experimentation in American Before the Second World War* (Baltimore: Johns Hopkins University Press, 1995).

[5] Cf. Richard W. Jackson (Roscoe's son) to Warren Weaver, 7 October 1949, plus enclosed endorsement, Rockefeller Foundation Archive, RG 1.1, Series 200D, Box 144, Folder 1778, RAC-NY. On Disney, see CCL to Roy Larsen, 5 November 1953, Box 12, Folder "L," JLA-BH. After several frustrated communications with Disney's associates, Little finally had

More than fifty years later, the "Great Bar Harbor fire" represents a relatively minor event in American history, and yet it raises many compelling questions for historians of science and culture. Why were such a large number of mice gathered in a little-known, nonprofit cancer research laboratory in Maine, and why did their animal deaths warrant national media attention alongside the direct effects of the fire on the human inhabitants of Mount Desert Island? Why did the NIH, as well as so many researchers and foundations, desperately want to reassemble JAX Lab and its mouse colony, and why did so few persons concerned with animal welfare or animal rights object to this project? Why was there more national financial support available for quickly rebuilding JAX's mouse houses than there was for rebuilding Bar Harbor's own natural resources (and thereby its local tourism industry)? And finally, why might Little have thought Mickey Mouse would prove a powerful tool for doing so—even while Walt Disney himself found this idea problematic?

This book seeks to answer these questions by examining the contingent process through which American biological and medical researchers developed the mouse into a standardized laboratory organism during the period from 1900 to 1955. Like the science it reconstructs, this book is based in large part on scientists' own accounts of their work—research articles, correspondence, and other bureaucratic paper trails of their administrative interactions—but it also mines the historical record for traces of this same science's more public culture: congressional testimony, publicity films, popular magazine feature writing, and so forth. By crafting a conversation between these rich bodies of primary and archival source material, it strives to explore the nature of laboratory mouse standardization from the perspectives of the animal's developers as well as its various users: mouse genetics experimenters in labs at JAX, medical researchers who paid to have JAX mice sent to their own labs, science policymakers who located a program for coordinating bench-top research in murine bodies, and the American public, who at once consumed laboratory mice as cultural icons of biological research and supported mouse experiments and production with their tax dollars. I situate my account at the locus of mass production that historians of technology have deemed "the consumption junction,"[6] but the engine driving my account is a concern for

lunch with Disney himself, "who seemed to be interested in incorporating the Laboratory's program and opportunities in connection with a television program which he is planning" (CCL to Benjamin Sherman, 5 April 1954, Box 12, Folder "S," JLA-BH). I have found no Disney program that meets this description and no further archival evidence that this collaboration progressed. See also C. J. LaRoche to Bea Little, 22 January 1954 Canning to LaRoche, 25 January 1954 and 4 February 1954, all Box 12, Folder "D (for Disney)," JLA-BH.

[6] Feminist historians first advocated this approach to highlight women's technological agency, as a corrective to accounts of early twentieth-century technologies made primarily

the complex interplay between science and society, so "users" is a theoretical category I employ very idiosyncratically. Taking cues, respectively, from the work of historians T. J. Jackson Lears and Phillip Pauly, I define "consumption" as a process of "individual choice and consciousness, wants and desires . . . in the context of social relations, structures, institutions, systems"—mainly because I am interested in perpetuating a definition of culture that emphasizes its historical and etymological roots at "the intersection of the biological and the technological" in America (especially during the early decades of the twentieth century).[7] Ultimately, then, this book describes the means by which scientists developed JAX mice into standard mammalian research organisms not just through the eyes of researchers doing experiments in laboratories, but through their encounters with the politicians and policymakers of the fledgling national system of biomedical research emerging in this period. At the same time, by considering how inbred mice became iconic symbols of the value of standardization within our culture's changing understandings of animals and science in the twentieth century, I am also suggesting that the public audience for this work must be considered another kind of scientific user. To understand how broader cultural imperatives shaped the practical nature of standardization in research, and vice versa, is to understand the social and scientific meaning of biology in twentieth-century American life.

Focusing primarily on the inbred mice produced by one institution—the Jackson Lab—my story chronicles both the specific evolution of one animal species (*mus musculus*, the common mouse) through its journey into the laboratory, as well as a key period of disciplinary and methodological reorganization in biology. Inbred strains were first developed and promoted for philanthropically funded cancer genetics research at the Jackson Lab, but financial deficits brought about by the Depression provoked director C. C. Little to circulate these animals more widely, as "pure" biological reagents for more diverse lines of medical research. After World War II, as the genetic etiology of cancer began to wane in experimental cancer work,

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from the perspectives of their mostly male creators and producers. Cf. Ruth Schwarz Cowan, "The Consumption Junction: A Proposal for Research Strategies in the Sociology of Technology," in *The Social Construction of Technological Systems: New Directions in the Sociology and History of Technology*, ed. Wiebe E. Bijker, Thomas P. Hughes, and Trevor J. Pinch (Cambridge: MIT Press, 1987), pp. 261–80, and the excellent and updated historiographic discussion in Nina E. Lerman, Arwen Palmer Mohun, and Ruth Oldenziel, "Versatile Tools: Gender Analysis and the History of Technology," and "The Shoulders We Stand on and the View from Here: Historiography and Directions for Research," in *Technology and Culture* 38 (1997): 1–32.

[7] Richard Fox and T. J. Jackson Lears, *The Culture of Consumption* (New York: Pantheon, 1983); Phillip J. Pauly, *Biologists and the Promise of American Life* (Princeton: Princeton University Press, 2000), p. 8.

the social and scientific need for good mammalian models of radiation damage gave the inbred mouse a new mission. Along with these changes in scientific agenda, however, came shifts in the patronage of science and the commercialization of its infrastructure (now including standardized lab animals). These developments nearly rendered the coexistence of research and mouse production at Jackson Lab unsustainable.

In the early years, JAX scientists constantly fought back the tide of what they came to know as "operation bootstrap"—the piggy-backing of mouse research onto the development of the production colony—but in retrospect, their persistence paid off. In the 1950s, although JAX was widely acknowledged as (in the words of one trustee) "the bureau of mouse standards," C. C. Little could barely convince either medical genetics researchers or granting agencies that mammalian genetics was worth much investment. Today sales of JAX inbred mice to outside researchers exceed two million organisms annually.[8] Furthermore, since its inception in 1959, JAX's frozen mouse embryo repository has accumulated more than 2,400 strains of mouse mutants. These animals, instead of being bred, are stored more cost effectively as embryos in vats of liquid nitrogen. Kenneth Paigen, Jackson Lab director from 1989 to 2000, claims that "more than 95 percent of all mouse models used in the world come from the Jackson Laboratory." As the 2001 JAX Annual Report concluded: "Researchers around the world agree that JAX© Mice are the 'gold standard' of genetic purity in mouse models," citing a 2000 report from Michael Festing and Elizabeth Fisher that "at least seventeen Nobel prizes . . . have flowed from the Jackson Laboratory."[9] One of these Nobel Prizes was awarded in 1980 to a JAX researcher, George Snell. Snell's congenic strains, which he began developing in the 1940s and completed in 1957, enabled him to identify and characterize the key genetic locus of histocompatibility in mice. This work (along with that of Baruj Benacerraf and Jean Dausset on the analogous phenomenon in human tissue transplant) was honored by the Nobel Committee as "laying the foundation for our knowledge of 'self' from 'non-self.' "[10]

[8] Personal communication, JAX Public Information Office, June 1992. See also Jackson Laboratory Annual Report, 1991.

[9] Lee Silver, "Suppliers of Mice," appendix A to *Mouse Genetics* (New York: Oxford University Press, 1995), p. 285. Paigen quoted in Diane Harrison, "Jax Lab Moves into the Future," *Ellsworth American*, 29 June 2000. Jackson Lab Annual Report, 2001, p. 26; cf. Michael Festing and Elizabeth Fisher, "Mighty Mice," *Nature*, 404, 6780 (20 April 2000): 815.

[10] Cf. introduction to George Snell, J. Dausset, and S. Nathenson, *Histocompatibility* (New York: Academic Press, 1976). When asked in 1996 about the medical significance of his work, however, Snell demurred: "Everybody hopes that what they do will turn out to be useful." Similarly, until his death in 1996, he continued to regale visitors with stories about how his Bar Harbor neighbors mistook news of "George winning the prize" as an

The Jackson Lab's research successes since the 1950s have not been limited to Snell's work. In the late 1950s and 1960s, for example, staff scientist Leroy Stevens was doing tumor transplantation work on Strain 129 mice, and he made a leap that would "profoundly affect stem cell technology a decade later." When Stevens noticed that the primordial germ cells that gave rise to teratomas looked a lot like the cells of considerably earlier embryos, he decided to transplant cells from various stages of early Strain 129 mouse embryos, including inner cell mass cells, into testes of adult mice. Some of these early embryo cells gave rise to teratomas, which, when transplanted into mouse bellies, displayed the ability to generate an impressive range of tissue types. Stevens called these cells that could support differentiation "pluripotent embryonic stem cells"—the origin of the term "stem cells."[11]

By far, however, one of JAX's proudest accomplishments is that the National Cancer Institute has renewed the lab's designation as a "Cancer Center" for genetic research every five years since it initially bestowed on JAX this honor in 1983. "That designation," Paigen wrote in his 2001 Annual Report Director's Message, "is vital to the Jackson Laboratory because basic cancer research is a thread woven into the fabric of our very institution."[12] For the twenty-five years between 1955 and 1980, that thread was not always acknowledged by science policy-making bodies, but it is one of the arguments of this book that it was there all along, ready to be rewoven (by new techniques of mammalian genetic manipulation) into the tapestry that is modern biomedical research. In fact, this book's pre-1955 focus highlights how problems of genetics once considered unanswerable in mammals were later transformed into cutting-edge research fields. Thus the Rockefeller Foundation program officer who in 1951 wrote that "the most valuable export of the Jackson Memorial Laboratory is in terms of boxes of mice rather than scientific publications" failed to appreciate the important, but often unpredictable, connections between the two. *Mus musculus* and its many mutants were well poised to colonize the laboratories of the new organismal molecular biologists of the 1970s, and work with mice has ranked especially significant in recent cancer research, as well as in the emergence of other biomedical fields such as molecular immunology and genetic epidemiology.[13]

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accolade for his gardening prowess, not his research accomplishment (interview with George Snell, May 1995, JLOH-KR).

[11] Quotes from Ricki Lewis, "A Stem Cell Legacy: Leroy Stevens," *The Scientist* 14 (5–6 March 2000): 19. Cf. Leroy Stevens, "The Development of Transplantable Teratocarcinomas from the Intratesticular Grafts of Pre and Post-implantation Mouse Embryos," *Developmental Biology* 21, 3 (March 1970): 364–82.

[12] Kenneth Paigen, "Director's Message," JAX Annual Report 2001, pp. 5–6.

[13] Scott Podolsky and Alfred Tauber, *The Generation of Diversity: Clonal Selection Theory and the Rise of Molecular Immunology* (Cambridge: Harvard University Press, 1977);

Ironically, even mammalian genetics—the field scientists and policymakers labeled too slow and laborious to invest in during the early twentieth century—has undergone what can only be described as an explosion in the last decade. The first mammalian gene ever cloned and sequenced was from a mouse.[14] Further, although mouse mutants have been the object of animal fanciers' fascination for centuries, the decoding of the mouse genome achieved in 2002 was possible because advances in mammalian gene manipulation technology (first recombinant DNA, then the gene "knock-out" technique[15]) combined with significant material investments, dating all the way back to the beginning of the twentieth century, to preserve genetically known strains of this animal created by and used in cancer research and radiation genetics. Mouse work has even begun to revolutionize basic Mendelian assumptions, especially the notion that a gene's expression is independent of the parental origin of the chromosome.[16]

Individual lives, however, are what connect larger structural shifts in the intellectual organization of science and the local modus operandi of research, and so it should not be surprising that I sustain my account of twentieth-century biology not through claims to institutional or organismic "greatness" but rather through more intimate knowledge of scientific biography. Thus I begin with and repeatedly emphasize the passion and drive of C. C. Little in the project of developing the inbred laboratory mouse.[17] During his testimony before the 1965 congressional hearings on cigarette labeling, Little asked lawmakers if they comprehended why he was focusing so much on the animal that was the basis of his scientific

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cf. Albert Cambrosio and Peter Keating, "The New Genetics and Cancer: Contributions of Clinical Medicine in an Era of Biomedicine," *Journal of the History of Medicine and Allied Sciences*, 56, 4 (October 2001): 321–52.

[14] D. A. Konkel, S. M. Tilghman, and P. Leder, "The Sequence of the Chromosomal Mouse Beta GLobin Major Gene: Homologies in Capping, Splicing and PolyA Sites," *Cell* 15 (1978): 1125–32.

[15] On recombinant DNA's development and regulation, Susan Wright, *Molecular Politics*: *Developing American and British Regulatory Policy for Genetic Engineering, 1972–1982* (Chicago: University of Chicago Press, 1994). Cf. Mario Capecchi, "Altering the Genome by Homologous Recombination," *Science* 244 (1988): 1288–92, and "The New Mouse Genetics: Altering the Genome by Gene Targeting," *Trends in Genetics* 5 (1989): 70–76.

[16] Shirley Tilghman, "The Sins of the Fathers and Mothers: Genomic Imprinting in Mammalian Development," *Cell* 96 (1999): 185–93.

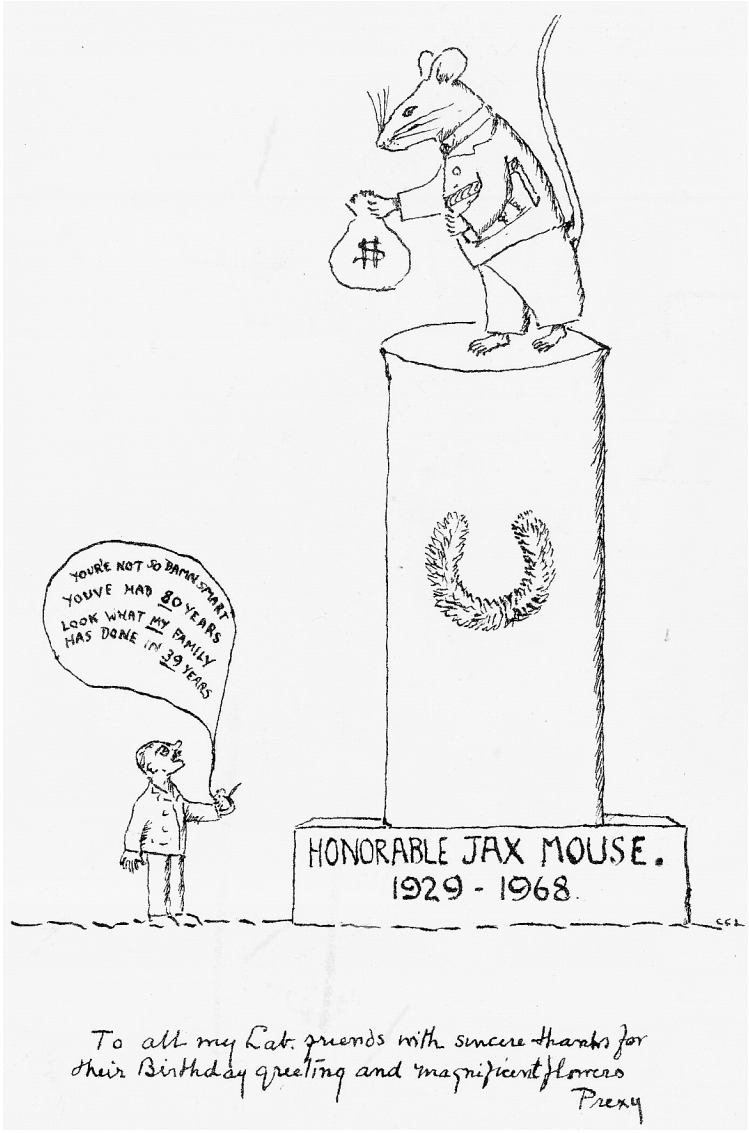
[17] For a biographical approach to model organisms, see Judith Johns Schloegel, "Intimate Biology: Herbert Spencer Jennings, Tracy M. Sonneborn, and the Career of American Protozoan Genetics," Ph.D. diss., Indiana University, forthcoming, and "Life Imitating Art, Art Imaging Life: Intimate Knowledge, Agency and the Organism as Aesthetic Object," *Videnskabsforskning* (Danish Newsletter for the Network of History and Philosophy of Science) 20 (1998): 2–18.

claims about smoking and cancer in humans: "I have spoken of mice as the servant of man. Why is this true? What made its truth evident? In other words, why mice?" Little was then nearing the end of a long career dedicated to "building a better mouse" for research, and his final project was controversial: as head of the Tobacco Institute Research Committee (precursor to the contemporary Council for Tobacco Research), he advanced the hypothesis that certain cancers developed in animals only if they possessed a preexisting genetic susceptibility. Indeed, there was perhaps no one for whom these queries held more personal meaning or urgency. On his eightieth birthday, Little penned a cartoon that summed up his views of the mouse's scientific and institutional achievements: it showed a likeness of Little himself dwarfed by a statue of the "JAX mouse, 1929–1968." The mouse carried a sack of money—presumably that which JAX made through the sales of mice to researchers—and addressed its scientist-muse: "You've had *80* years! Look what *my* family has done in *39* years!"[18] (fig I.5).

Little's question, "why mice?" did not merely reflect his own inner journey. Taken as a broader reflection, this query interrogates the central role of particular animals in the process of biological and medical knowledge-making. Exactly how and why are certain animals chosen for certain kinds of experimental research, while other creatures and other compelling research questions ignored? Most scientists who work with laboratory mice respond to the material part of this question by citing a "laundry list" of their creatures' many research-friendly biological properties. For example, they are small and relatively tame animals, which makes them easy to handle, house, and feed. They breed readily and often (several times per year), and three weeks after the females have mated, good-sized litters of pups are born, which allows for a quick yield of research results, whether in terms of providing a large sample or observing generational patterns. Finally, mice are mammals with a 99 percent genetic homology to humans, and they happen to get many of the same diseases as us (cancer, heart disease, etc.), which (by extrapolation) makes it possible to track and experiment on many human health conditions in situ.[19]

[18] C. C. Little, typescript, 1965 Testimony on the Cigarette Labeling Hearings (n.d.), Box 732, CCL-UMO. On Little's involvement with the TIRC, see Robert N. Proctor, *Cancer Wars* (New York: Basic Books, 1995), p. 107; cf. Little's eightieth birthday cartoon in Jackson Laboratory Photo Archive.

[19] See, for example, Patricia Lauber, *Of Man and Mouse: How House Mice Became Laboratory Mice* (New York: Viking Press, 1971), p. 49; Gina Kolata, "A Star Is Born: Even a Lab Mouse Needs an Agent," *New York Times*, 26 January 1997, p. E5; cf. Lee Silver, "Mice as Experimental Organisms," *Encyclopedia of the Life Sciences* (Nature Publishing Group, 2001), available at www.els.net (accessed 8 June 2003). The figure of 99 percent genetic homology comes from recent Mouse Genome Project data—e.g., Mark S. Boguski, "The Mouse That Roared," *Nature* 420 (5 December 2002): 515–16.



I.5. Cartoon drawn by C. C. Little to thank staff for their celebration of his eightieth birthday [Source Credit: Jackson Laboratory Archives].

From a scientist's perspective, enumerating such variables provides a concise statement of the important pragmatic qualities of a successful experimental animal in biomedicine. But from a historian's perspective, these seemingly universal measures of scientific success work to decontextualize the mice themselves from the places and the circumstances under which they were developed and used as experimental animals. By presuming that the contemporary understanding of what constitutes "good" research is timeless, they "black box" the values informing the research process and render invisible the very nexus of politics and practices that defined what counted as laboratory "success" (and therefore, which intrinsic qualities of the mouse were "useful") in the first place. Mice that entered scientific laboratories before 1900 were far more likely to be stray creatures looking for food or shelter. By 1960 mice had become laboratory fixtures in cancer studies and mammalian genetics (especially radiation genetics) embedded with multiple, co-existent meanings of their "usefulness." The former were animals trying to further their own basic survival. The latter were animals whose bodies and representations were re-engineered by humans, to further the local goals of particular research communities as well as the social aims of those people and institutions that surrounded and supported this work—including other scientists, foundations, and members of the American public. In short, what remained of their animal agency in the human world was far more complex than simply searching for scraps of food or warm shelter.

Spurred on by Robert Kohler's 1994 book *Lords of the Fly*, as well as by recent science studies work in the material cultures of experiment, both biologists and historians of biology are now paying attention to the role of model organisms. Some of this work follows the model of "great men" histories of science but substitutes "great organisms." But the bulk of it has yielded important new insights with regard to the social life of biologists in their laboratories, as well as the process of making biological knowledge. Developing model organisms—from flies, to corn, to bacteria, and eventually to viruses—was (and still is) one of the most resource-intensive aspects of being a geneticist in the early twentieth century. But seemingly mundane investments in these tools of the trade have yielded many rewards for both the individual and the collective enterprise: faster research results and greater consensus over their meaning, to name just two.[20]

[20] Robert E. Kohler, *Lords of the Fly: Drosophila and the Experimental Life* (Chicago: University of Chicago Press, 1994); Rachel Allyson Ankeny, "The Conqueror Worm: An Historical and Philosophical Examination of the Use of the Nematode *Caenorhabditis Elegans* as a Model Organism," Ph.D. diss., University of Pittsburgh, 1997; Ilana Löwy and Jean-Paul Gaudillére, "Disciplining Cancer: Mice and the Practice of Genetic Purity," in *The Invisible Industrialist* (New York: Macmillan, 1998), 209–49. Cf. Adele E. Clarke and Joan H. Fujimura's collection, *The Right Tools for the Job: Materials, Instruments, Tech-*

Model organism studies have also provocatively explored the relationship between human and material agency in the triumph of experimental biology over earlier natural history methodologies. Kohler, for example, argues that *Drosophila* "colonized" genetics laboratories by virtue of its natural fecundity. The fly's ability to generate new mutant forms of itself catalyzed T. H. Morgan and his colleagues to standardize and domesticate a variety of strains for chromosome mapping, and the subsequent deluge of experimental material displaced rival neo-Mendelian studies and organisms from biology's center stage. Angela Creager's analysis of the history of TMV (Tobacco Mosaic Virus) proposes another means of understanding the discipline's transformation—namely, through attending to the "everyday practice of finding and identifying workable precedents for innovative experiment." Wendell Stanley and other viral researchers, she argues, transformed biology by developing TMV into "a cluster of possible models and templates"—from the conceptual (viruses as genes) to the technical (viruses as crystallized proteins)—which themselves became a "set of resources for the creative borrowing and elaboration of previously unseen analogies" across diverse and unconnected fields, such as cell biology, cancer research, and bacterial genetics.[21]

Much of this work, however, still locates the value of standardized model organisms in universalized norms of scientific practice, rather than in particular means through which these creatures were first cultivated. As Adele Clarke notes in an insightful early essay: "In order to observe or produce the phenomena they study, all working scientists must obtain and manage research materials."[22] But standardization is often presumed to be an obvious next step in this process, undertaken to manage the

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niques and Work Organization in Twentieth Century Life Sciences (Princeton: Princeton University Press, 1992), especially the essays on corn by Barbara Kimmelman and on Planaria by Gregg Mitman and Anne Fausto-Sterling; Andrew Pickering, ed. *Science as Practice and Culture* (Chicago: University of Chicago Press, 1992); Pickering, *The Mangle of Practice: Time, Agency, and Science* (Chicago: University of Chicago Press, 1995). For an excellent overview of recent work on model organisms, with careful attention to issues of agency and the material culture of experimental more broadly, see chapter 8 of Angela N. H. Creager, *The Life of a Virus: TMV as an Experimental Model, 1930–1965* (Chicago: University of Chicago Press, 2001). For a scientific perspective on model organisms, see the "Biology's Models" special issue of *New Scientist*, vol. 17, sup. 1 (5) (2 June 2003).

[21] Kohler, *Lords of the Fly*; Creager, *Life of a Virus*, pp. 6, 328–29.

[22] Adele E. Clarke, "Research Materials and Reproductive Science in the United States, 1910–1940," in *Physiology in the American Context, 1850–1940*, ed. Gerald L. Geison (Bethesda: American Physiological Society, 1987) p. 323. Howard Gest makes a similar point about the term "model" in science: see his "Arabidopsis to Zebrafish: A Commentary on the 'Rosetta Stone' Model Systems in the Biological Sciences," *Perspectives in Biology and Medicine* 39 (Fall 1995): 77–85.

natural "complexity and diversity of living organisms" and thereby simultaneously make the experimental systems in which biologists use them more "productive" while tending to the "practicalities . . . of scientific careers."[23] These assumptions are even made within historical accounts that (unlike scientists' "laundry lists") explicitly acknowledge the importance of local decision making in the development, dissemination, and adaptation of model organisms. Existing narratives beg larger questions about the underlying values motivating the process of adopting standardized animals and other model systems at the bench-top: "Complex" compared to what? "Manageable" and "practical" for whom, and why? "Productive" to what ultimate end?[24]

Recent case studies of standardization in the history and sociology of science stress how—for everything from techniques and instruments to classification and building schemes, and even human organ donation—achieving standards requires intense negotiation over what material, organizational, and conceptual categories can and should be deliberately controlled and therefore taken for granted.[25] Standardized organisms, therefore, need to be reconceived within a broader sociology of technoscientific work. These animals are the result, rather than the cause, of consensus among early twentieth-century experimental biologists, and a key goal of

[23] Creager, *Life of a Virus*, p. 319; Kohler, *Lords of the Fly*, p. 206.

[24] To counteract what he sees as a "hegemony of theory" in the social studies of science, Hans-Jorg Rheinberger has developed an epistemology of experimentation that treats research as a process simply for producing "epistemic things." See *Towards a History of Epistemic Things: Synthesizing Proteins in a Test Tube* (Stanford: Stanford University Press, 1997). My account counteracts what I see as another hegemony, namely, that of presumed universal scientific values.

[25] With regard to biology and standardization, see Kathleen Jordan and Michael Lynch, "The Sociology of a Genetic Engineering Technique: Ritual and Rationality in the Performance of the 'Plasmid Prep' "; Patricia Peck Gossel, "The Need for Standard Methods: The Case of American Bacteriology"; and Peter Keating et al., "The Tools of the Discipline: Standards, Models, and Measures in the Affinity/Avidity Controversy in Immunology," all in *Right Tools*, ed. Clarke and Fujimura, pp. 77–114, 287–311, 312–56, respectively. On the broader philosophical and sociological implications of standardization for science and technology, see Joan H. Fujimura, "Crafting Science: Standardized Packages, Boundary Objects and 'Translation,' " in *Science as Practice and Culture*, ed. Pickering, pp. 168–211; Theodore Porter, "Objectivity as Standardization: The Rhetoric of Impersonality in Measurement, Statistics and Cost-Benefit Analysis," in *Rethinking Objectivity*, ed. Allan Megill (Durham: Duke University Press, 1994), pp. 197–237; Linda Hogle, "Standardization Across Non-Standard Domains: The Case of Organ Procurement," *Science, Technology, and Human Values* 20, 4 (1995): 482–501; Geoffrey Bowker and Susan Leigh Star, *Sorting Things Out: Classification and Its Consequences* (Cambridge: MIT Press, 1999); Amy E. Slaton, *Reinforced Concrete and the Modernization of American Building, 1900–1930* (Baltimore: Johns Hopkins University Press, 2001).

this book is to map the historical credibility of the notion of "standardization" through the story of the mouse's development in the laboratory. What have been the values of those who pursued standardization of laboratory animals, and to what end? How did they convince others of the rightness of their methods and goals?[26]

As Kohler notes, one common-sense understanding of "standard" is simply "the things that everybody uses."[27] This definition plays on the primary meaning of the word, dating from fifteenth-century debates over weights and measures: a standard is an exemplar, an object or quality that serves as the authorized basis or principle to which others conform or by which they are judged.[28] In experimental biology, the material and practical aspects of "standardization" are synchronic, regardless of which is primary. For example, widespread research use of a species (one important practical concern) correlates with the extent to which that organism is first available or capable of being produced in large numbers (two key material achievements). In the case of genetically standardized mice, the number of animals in circulation started rising in the 1930s, and the creatures now represent (along with genetically standardized rats) at least 70 percent of all animals used in research.[29]

Still, in retrospect, the early success of the inbred mouse was underdetermined at the level of research practice; that is, its initial users did not necessarily commit to the genetic framework of experimentation in order to utilize this animal as a meaningful research tool. As Rachel Ankeny argues in her study of the nematode worm, *C. elegans*, model organisms

[26] The notion of mapping historical credibility I take from Simon Schaffer, "Accurate Measurement Is an English Science," in *The Values of Precision*, ed. M. Norton Wise (Princeton: Princeton University Press, 1995), p. 136 ("Undoubtedly a Victorian value, precision badly needs a cultural history which maps its historical credibility rather than assuming its methodological validity.") In this pursuit, my work is deeply indebted to earlier sociologists of standardization, in particular "social worlds" theorists. See introduction to Joan Fujimura, *Crafting Science: A Sociohistory of the Quest for the Genetics of Cancer* (Cambridge: Harvard University Press, 1996).

[27] Kohler, *Lords of the Fly*, p. 14.

[28] On the history of the word "standard," see the *Oxford English Dictionary*, which traces this usage to a 1429 parliamentary debate. For some interesting reflections on the history of standardization more broadly—especially regarding early French debates over state standardization of military production—see Ken Alder, *Engineering the Revolution* (Princeton: Princeton University Press, 1997).

[29] The numbers of animals are from the USDA/APHIS census of 1983 because the more recent census has not been released to the public. See U.S. Congress, Office of Technology Assessment, *Alternatives to Animal Use in Research, Testing, and Education* 5 (Washington, DC, 1986). On the standardization of the rat, which followed a parallel but very different scientific path from the mouse, see Bonnie Tocher Clause, "The Wistar Rat as a Right Choice: Establishing Mammalian Standards and the Ideal of a Standardized Mammal," *Journal of the History of Biology* 26 (Summer 1993): 329–49.

often serve as important vehicles of problem clarification—either for exploring new lines of work or for promoting a particular approach to biological work that is transferable *across* many different areas of research. Little clearly envisioned the inbred mouse as a vehicle for the latter—he sought to promote genetic approaches to *all* biomedical research—but both intellectual and practical constraints limited the straightforward achievement of this vision. The current meaning of gene (as functional piece of DNA) had not yet emerged in 1938, when Little gave a conference talk on "Some Contributions of the Laboratory Rodent to Our Understandings of Human Biology," and even when it did emerge, chromosomal manipulation in mammals proved technically impossible before recombinant DNA in the 1970s. One important historical question, then, is how did the standardization of the mouse at the locus of the gene become second nature (materially speaking) for biologists during a time when (practically speaking) precision control of mouse genes could not be experimentally achieved? In other words, how did the genetically standardized mouse initially succeed as a standard organism when mammalian genetics, the very science for which it was supposedly best designed, initially did not?[30]

My analysis attempts to resolve this paradox by resurrecting an even earlier meaning of "standard," originating in medieval warfare: a conspicuous object, such as a banner, carried at the top of a pole and used to mark a rallying point.[31] Of course, the ubiquity of these animals was what would literally make them conspicuous—as Little himself put it, mice had "served the avid maul of genetic researchers long and well" enough by 1938 to be granted a "titular partnership at a scientific meeting."[32] But while geneticists collected and developed more than fifty years' worth of genetically known mouse strains, without being able fully to exploit these materials for their own analyses, researchers found alternative uses for the animals. Some of these uses, such as tumor transplant studies, Little himself promoted, but others, such as the specific locus test, he did not and could not have imagined when he first began inbreeding the creatures. JAX mice,

[30] Steward Brand, *How Buildings Learn: What Happens to Them After They're Built* (New York: Penguin, 1995), p. 2.

[31] The 1989 OED notes that in 1138 the "standard" was so-named from " 'stand' because, it was there that valour took its stand to conquer or die." For science studies scholars, this rhetoric of warfare will invoke Bruno Latour's version of actor-network theory—see *The Pasteurization of France*, trans. Alan Sheridan and John Law (Cambridge: Harvard University Press, 1988)—although this is appropriate because this usage resonates with the rhetoric the historical actors themselves employ to describe the mouse's usefulness—e.g., for "the war on cancer." Cf. Wise, "Introduction," in *The Values of Precision*.

[32] C. C. Little, "Some Contributions of the Laboratory Rodent to Our Understanding of Human Biology," *American Naturalist* 73 (1939): 127–38.

then, functioned less as static research tools guaranteeing the dominance of a particular line of work than as ever-present totems of the genetic approach in American experimental biology. Because they were standardized at the locus of the gene, considerations of how their hereditary constitutions shaped results became a material part of all work in which they were used. But whether genetic considerations were made explicit by mouse researchers is itself a historically specific phenomenon that cannot be explained away at the level of what was technically possible or impossible. As genes have become increasingly valued entities in both American biology and American culture over the last hundred years, inbred laboratory mice have become increasingly valued for their ability to measure genetic effects.[33] My claim, then, is that the emergence of standard research organisms reflects changing social and disciplinary ecologies of knowledge. Genetically standardized mice were the standard-bearers for a genetic approach to biomedicine; their production represented, to paraphrase Karl Marx on technology, the power of genetic knowledge objectified.[34]

In making this argument, I do not mean to exaggerate the homogeneity of biological and medical research practices. In the early twentieth century, just as now, even biologists who openly embraced a genetic approach did not always agree on what Frederick Winslow Taylor called "the one best way."[35] Over the last hundred years researchers have argued frequently and vehemently over which kind of organisms are the right tools for research, the most famous sound bite from these debates being Jacques Monod and François Jacob's bold declaration: "anything found to be true of *E. coli* must also be true of elephants."[36] These controversies reflect genuine epistemological and methodological disagreement within the

[33] Economists and historians of mathematics often make this point about measurement more generally. See Ann Jennings, "The Social Construction of Measurement: Three Vignettes from Recent Events and Labor Economics," *Journal of Economic Issues* 35, 2 (2001): 365–71 (thanks for Marilyn Power for this reference): Theodore M. Porter, *Trust in Numbers: The Pursuit of Objectivity in Science and Public Life* (Princeton: Princeton University Press, 1995).

[34] "Nature builds no machines, no locomotives, railways, electric telegraphs, self-acting mules, etc. These are the products of human industry; natural material transformed into organs of the human will over nature, or of the human participation in nature. *They are organs of the human brain, created by the human hand*; the power of knowledge objectified." Karl Marx, *Outlines of the Critique of Political Economy*, 1857–61, trans. Martin Liclaus (New York: Penguin Books, 1973), p. 706. (Thanks to Shahnaz Rouse for pointing out this connection.)

[35] Cf. Robert Kanigel, *The One Best Way: Frederick Winslow Taylor and the Enigma of Efficiency* (New York: Viking, 1997).

[36] Jacques Monod and Francois Jaçob, "General Conclusions: Teleonomic Mechnisms in Cellular Metabolism and Growth," *CSH Symposium on Quantitative Biology* 26 (1961): 393.

community of practicing biologists. Should model organisms be simplified models of real life, as bacterial geneticists and *C. Elegans* workers often argue, or bits of real, complex life on which we can experiment, as mouse workers claim? Where individual biologists come down on these questions depends in large part on what jobs they think the discipline of biology itself should be doing. In 1975, for example, physiologist Hans Krebs championed the "unique characteristics" rationale articulated by August Krough in 1929 for choosing laboratory organisms: "for a large number of problems there will be some animal of choice . . . on which it can be most conveniently studied." But while Krough originally saw this as reason to pay attention to zoological diversity, Krebs assumed such diversity was "an exception, against a background of presumed generality."[37] Likewise, Gunther Stent has argued that in the 1960s a whole generation of young molecular biology researchers turned back to larger organisms and problems of development, largely because they believed that all the simple problems of the field had already been solved and it was time to move onward and upward (simultaneously in the chain of being and in their professional standing).[38]

Historically, however, model organism debates among biologists have overshadowed the equally important points of consensus that necessarily existed among biologists who worked on different organisms, as well as between the scientists who created and used standardized organisms and those supporting their work. Sometimes these concordances in values found voice, such as in government and foundation policy debates over what kinds of biological research, and therefore what kinds of organisms, to fund in postwar biomedical research. Nearly every scientist and policymaker in the late 1940s and 1950s—from those working on mice at the National Cancer Institute to those leading the Atomic Energy Commission's biological research projects in *Drosophila* and Paramecium—agreed that some sort of laboratory animal research was necessary to establish valid claims about everything from human cancers to genetic "fallout." The key question they disagreed on was: what kind would prove the most convincing? Scientific values of experimental proof had to be reconciled with political values of expediency and overall research coordination, but more often than not, even this was achieved without rancor.

[37] For a trenchant historical analysis of the Krough principle, see Cheryl A. Logan, "Before There Were Standards: The Role of Test Animals in the Production of Empirical Generality in Physiology," *Journal of the History of Biology* 35 (2002): 329–63, quote on 329–30.

[38] Soraya de Chadarevian, "Of Worms and Programmes: 'Caenorhabditis elegans' and the Study of Development," *Studies in the History and Philosophy of the Biological and Biomedical Science* 29 (1998): 81–105.

As Evelyn Fox Keller has argued, this scenario is not surprising: "by scientists' own internal ethic," results "must provide at least some predictive success to remain satisfying; and by the social and political ethic justifying their support, this predictive success must enable the production of at least some of the technological 'goods' the public thinks it is paying for." But more often than not, consensus in mouse research passed silently, either because the only historical actors to whom it would have seemed controversial literally had no voice—such as the mice who were being experimented on—or because the consensus among the human beings involved was so great that it seemed not to require comment. A final goal of this book, then, is to reinstate some of these "critical silences" in the consensual historical discourse of developing model organisms—in particular, those related to the scientific and social values informing animal research.[39]

For the historian, this approach presents a problem of sources as well as interpretation. One reason why scientific and technological controversies are so well-studied is that the day-to-day consensus assumptions that structure work in these fields are much more difficult to document. There are precious few "smoking guns" to be found that enable one to pinpoint the origin and development of agreement in areas where there was never any questioning of received values.[40] Nevertheless, agreed-upon values were important resources that biologists and policymakers used to articulate what jobs needed doing with laboratory mice and how they should do them. It is not just a coincidence, for example, that the initial funding for the development of the Jackson Lab's "mouse factories" came from Detroit car makers, who embraced the ethos of mass production. Nor is it immaterial that Little could speak, in a 1937 *Life* article, of mice as "Replac[ing] Men on the Cancer Battlefield" without fear of retribution from animal welfare groups.

In turn, I consider standardized laboratory mice not only as artifacts of particular knowledge-making activities but as what Ian Hacking has called *forms* of scientific knowledge—"what is held to be thinkable, or

[39] Evelyn Fox Keller, "Critical Silences in Scientific Discourses: Problems of Form and Re-Form," in *Secrets of Life, Secrets of Death* (New York: Routledge, 1992), pp. 91, 85. My historical approach to this problem neglects, but does not deny, the mice themselves as important "silent actors"; for a sociological analysis (and problematization) of agency in animals and other actors of the natural world, see Michel Callon, "Some Elements of a Sociology of Translation: Domestication of the Scallops and the Fisherman of St. Brieuc Bay," in *Power, Action, Belief: A New Sociology of Knowledge?*, ed. John Law (New York: Routledge and Kegan Paul, 1986), pp. 196–229.

[40] Pam Scott, Eveleen Richards, and Brian Martin, "Captives of Controversy: The Myth of the Neutral Social Researcher in Contemporary Scientific Controversies, " *Science, Technology, & Human Values* 15, 4 (Fall 1990): 474–94.

possible, at any given moment"—and my account strives to recover historical traces of what linguistic, material, and conceptual potentials were tapped while decisions about these animals' development and use were being made, both inside and outside the laboatory.[41] Ultimately, I argue that the usefulness of standardized laboratory mice was settled through consensus, not necessarily over the creatures' uses in specific experiments (although there was some of this), but over their ability to negotiate two key underlying tensions in life-science work of the early twentieth century.

The first tension is that between natural and technological systems in the realm of biological experiment. Vast controlled breeding populations of inbred mice, like many other living tools of basic biological research, would not exist save for the efforts of human scientists, so one key question facing those who used them involved how much of the knowledge obtained reflects aspects of mouse biology as it really is, and how much is an artifact of the experimental system. This question was raised repeatedly by the scientific actors themselves—sometimes by those with research programs that competed with Little's genetic vision (e.g., Maud Slye's pedigree approach to mouse cancer research during the 1920s), and other times by those who shared it (e.g., William Russell's specific locus test in radiation mutation studies during the 1950s). My narrative pays close attention to such liminal moments in this debate because they are the points at which scientific consensus was literally articulated. But it is also important for the larger argument of this book to note that the natural truths about the animal under discussion were framed by consequences beyond the laboratory. In the case of the Slye-Little debate, at stake was the institutional and intellectual framework for future cancer research funding: centrally coordinated, theoretically informed projects favored by Little and most experimental biologists, or locally centered, clinically framed case studies preferred by Slye and most medical researchers. In the case of Russell, it was the developing relationship between basic biological research and radiation policy-making in postwar America: would researchers themselves play a direct role in making policy, or would they merely present their data? These contexts, then, defined the intellectual, political, and social possibilities within which mouse users staked out their knowledge claims. The relatively peaceful coexistence of different mouse meanings within and between them suggests that persistent heterogeneity can stabilize (rather than undermine) projects to standardize scientific knowledge and the tools of its practice.[42]

[41] Ian Hacking, "Weapons Research and the Form of Scientific Knowledge," *Canadian Journal of Philosophy*, supp. vol 12 (1987): 237–60, quote on 243.

[42] A similar point with regard to laboratory techniques is made by Jordan and Lynch in "The Sociology of a Genetic Engineering Technique."

The second tension is that between human and animal subjects in the realm of American culture. This is an especially interesting theme that deserves its own history, especially in reference to scientific experimentation.[43] What animals are enough like us to make laboratory results obtained from them generalizable to humans, but not so much like us that we ethically prohibit their being the subjects of experiments? Social assumptions have shaped scientific considerations and uses of animals in this regard—particularly for dogs and other sentimentally valued creatures. Diane Paul details how the Rockefeller Foundation's Alan Gregg launched a postwar study of "Genetics and Social Behavior" in dogs because he sought to demonstrate to educators and doctors, the heritability of behavioral traits but recognized that existing work "had been demonstrated in organisms—such as fruit flies and rats—to which few persons could relate to emotionally." Also, Susan Lederer demonstrates that medical researchers at the Rockefeller Institute for Medical Research eliminated full-body photographs of laboratory dogs, as well as textual reference to their names, in published journal articles; in these ways, she argues, they achieved "the invisibility of the 'naturalistic' animal" and therefore shielded themselves from the criticisms of animal welfare advocates.[44] Occasionally, this tension was explicitly articulated or referenced by historical actors in the mouse's story—for example, in some of Little's many public appeals for mouse cancer research, or in debates by the Biological Effects of Atomic Radiation (BEAR) committee over radiation data in seven-locus mice versus Japanese atomic bomb survivors—and my analysis exploits these rare self-conscious reflections. But I also formulate this part of my argument comparatively, referencing existing case studies of other extrapolation debates in animals whenever possible, in lieu of referencing a broader cultural and conceptual history of the use of animal subjects in science that has yet to be written.[45]

Finally, a few words on my view of biologists who use mice and their work. Laboratory mice occupy a prominent place within recent biomedi-

[43] Susan Lederer's work on the history of human experimentation, *Subjected to Science*, is very attentive to this theme.

[44] Diane Paul, "The Rockefeller Foundation and the Origins of Behavioral Genetics," in *The Expansion of American Biology* (New Brunswick: Rutgers University Press, 1991), p. 273; Susan Lederer, "Political Animals: The Shaping of Biomedical Research Literature in Twentieth Century America," *Isis* 83 (1992): 61–79.

[45] Some more recent sociological monographs make important contributions to this goal: see, for example, Eileen Crist, *Images of Animals: Anthropomorphism and the Animal Mind* (Philadelphia: Temple University Press, 1999); Arnold Arluke and Clifford Sander, *Regarding Animals* (Philadelphia: Temple University Press, 1996). For a historical approach, see Daniel Todes's masterful account of Pavlov's dog experiments: *Pavlov's Physiology Factory:*

cal success stories: contemporary Americans need only open a major daily newspaper or listen to a national television news program to encounter the work now being done with these rodents—as animal models for the genetics of Alzheimer's disease or intelligence, to cite just a few recent reports. Perhaps in response to such developments, North American animal rights and environmental activists have begun to pay attention to mice in laboratories. In 1999 the Animal Legal Defense Fund called for a revision in the definition of "animal" covered by the 1972 version of the Animal Welfare Act, citing the "arbitrary" discretion exercised by the then-secretary of agriculture not to include the mice and rats in scientific laboratories among those animals covered when he first administered the act in 1966. Despite winning this suit, the U.S. Senate quietly approved a measure in February 2002 that would eliminate the federal funding necessary to change the regulations, setting the stage for a "tough battle" between university scientists and animal rights activists.[46] Likewise, in 2000 the Canadian Patent Office filed an appeal on the Canadian Federal Court of Appeal's decision to allow Harvard researchers a patent on Oncomouse in 1986. The commissioner of patents argued that the current Patent Act does not permit patenting higher life forms such as plants and animals, and in its most recent ruling on the case, the Supreme Court of Canada (by a 5–4 decision) agreed with him.[47]

My interest in documenting how standardized laboratory animals came to be is both academic and political, but not condemnatory. That current resistance to C. C. Little's "new deal for mice" took decades to materialize speaks to how mouse use in science has indeed become a "black box," in both science and society, but perhaps now is the perfect time to reopen that box.[48] How researchers and their constituencies determine what scientific things—objects, methods, theories—can be taken for granted reveals something very important about the nature of their work, as well as about received cultural values. My hope is that by returning to a time

Experiment, Interpretation, Laboratory Enterprise (Baltimore: Johns Hopkins University Press, 2002).

[46] See "Animal Welfare: A Petition for Rulemaking," *Federal Register* 64, 18 (28 January 1999): 4356–67. Cf. Ron Southwick, "Senate Votes to Block Expansion of Lab-Animal Regulations," *Chronicle of Higher Education*, 1 March 2002, p. 25; "Researchers Face More Federal Scrutiny on Animal Experimentation," *Chronicle of Higher Education*, 28 June 2002, p. 23.

[47] "Harvard College v. Canada (Commissioner of Patents)," 2002 Supreme Court of Canada 76, file no. 28155; 2002: May 21; 2002: December 5.

[48] As Geoffrey Bowker and Susan Leigh Star suggest in their work on standardization, "Black Boxes are necessary and not necessarily evil. The moral questions arise when the categories of the powerful become taken for granted." See Bowker and Star, *Sorting Things Out*, p. 320.

when the existence and use of these creatures first took shape, especially to Little's prescient vision of mouse use, we may learn more about how human agency shapes the course of science. In this way, we can better appreciate the scientific knowledge obtained from mice for what it is (as well as what it is not) and perhaps even begin envisioning new ways to make biomedical science a livable and workable space for all animals—human and nonhuman—to inhabit.