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Essay review

Of mice and men and low unit cost

Making mice: Standardizing animals for American biomedical research, 1900–1955. Karen A. Rader; Princeton University Press, Princeton, NJ, 2004, pp. 312, Price $45.00 £29.95 hardback, ISBN 0-691-01636-4.

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1. Introduction

Making mice is a contribution to scientific biography, to the history of laboratory model organisms, and to the historiography of scientific standardization. The heart of the story is the development of standardized mice (i.e. genetically inbred strains) for use in cancer research, basic mammalian genetics, and other allied lines of work. One theme is the work of learning how to create such strains through careful breeding and husbandry. Another is building the organization which can produce and distribute strains on a fairly substantial scale. This organization was (and is) both a world of volunteers and a formal bureaucracy. A third part of the story is the development of alliances with significant players and social worlds—the medical cancer research world, mouse fanciers, animal rights people, government agencies, private philanthropic foundations and individuals, the press, and consumers of biomedical products and services.

Rader's argument is organized around the story of Clarence Cook Little's career as a mammalian geneticist at the dawn of American genetics. She follows Little from his student days inbreeding mice to produce genetic homogeneity, sparring with fly geneticists like Sturtevant and Morgan over the interpretation of data, and becoming interested in the relevance of inbred mice to the study of cancer. Little's career took him from junior scientist–administrator at Cold Spring Harbor, to president of two universities, and finally to founding director of the Jackson Memorial Laboratory in Bar Harbor, Maine. A curious coda to Little's life of science entrepreneurship, upon his retirement in 1956,

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was his position as science advisor to the Tobacco Industry Research Council. Little's career is intertwined both with the institutional and organizational biography of the Jackson Lab and with that of *Mus musculus*, the domestic house mouse, in its own career path from pest and pet to mass produced, standardized, genetically purified, specialized laboratory 'tool' or 'reagent' for American biomedical science. During Little's lifetime, 'the mouse' became a model organism for the genetics of cancer, tumor transplantation, immunogenetics, and radiation biology.

2. C. C. Little and the Jackson laboratory

Clarence Cook Little (1888–1971) was a student at Harvard during the first decade of the twentieth century, just as genetics was becoming a new discipline. His undergraduate interest in dog breeding shifted to mouse genetics under the tutelage of pioneer mammalian geneticist William Castle. Little continued at Harvard as a graduate student with Castle at the Bussey Institute of Applied Biology to become one of the first mouse geneticists, focusing on the development of inbred strains for the Mendelian analysis of coat and eye color mutations. Little brought mice into the laboratory and contributed to their transformation into laboratory materials, as C. W. Woodworth, F. W. Carpenter, and F. J. Moenkhaus (Castle students) and F. E. Lutz (influenced by Castle's inbreeding studies with fruit flies), were doing for Drosophila (Allen, 1975). Little's work began, not with 'wild' caught flies on window ledges, but with animals purchased from mouse fanciers, whose interests in exotic coat colors and whose commercial husbandry practices provided a ready source of raw materials.

Little's early interest in standardization of research materials can be traced to his undergraduate project. Johannsen's theory of pure lines appeared in 1909, implying genotypic limits to the power of natural selection and raising new questions about effects of inbreeding (Johannsen, 1909). Inbreeding was thought to lead to genetic homogeneity and to potentially harmful side effects such as reduced fertility. But homogeneity could also be viewed as genetic purity, sustainable by careful husbandry practices and controlled inbreeding. With the rise of genetics as a new analytic discipline in biology, geneticists argued that genetically pure or homogeneous materials were needed in all kinds of biological research to disentangle genetic from other kinds of effects (e.g. Morgan 1926). So, if the side effects were tolerable, inbreeding could become a means of genetic purification of research materials and thus the basis for standardizing genetic backgrounds against which to carry out various kinds of scientific work. By the time Little completed his graduate work on mouse coat color genetics (and after failing his exams in 1912), he became established as a mouse geneticist, introducing Mendelian nomenclature for strains derived from the fanciers (p. 41).

Little's interests, however, were already shifting to the use of mice for cancer research. Studies of spontaneous tumors in mice were linked to genetic questions by E. E. Tyzzer, director of the Harvard Cancer Commission of the US Public Health Service. Tyzzer examined susceptibility to tumors as a result of tissue transplanted between mouse strains. Little attempted to interpret Tyzzer's results in terms of a Mendelian multifactor explanation of cancer susceptibility and argued that such results would only be interpretable if the strains used were genetically homogeneous (an argument that Thomas Hunt Morgan extended in 1926 to the study of developing embryos generally). This argument for genetic purity of research materials became central to Little's lifelong scientific and entrepreneur-

ial agendas. Little went to work for Tyzzer for a short while before serving in the military during World War I and then taking a position in 1919 at Cold Spring Harbor's Station for Experimental Evolution, which was founded by Charles Davenport, Castle's mentor (p. 50).

At Cold Spring Harbor, Little continued his cancer interests, but also began the organizing activities that eventually transformed his skills as an 'inbreeder' into those of a manufacturer of purified mice and purveyor of standards. He started the Mouse Club of America in 1920 to formalize the exchange of information and material for scientific mouse breeding. In 1922, Little's career took an administrative turn when he accepted the presidency of the University of Maine and then three years later the presidency of the University of Michigan. Four years after that, Little left academia to found the Jackson Memorial Laboratory in 1929. In all three places, Little attempted to continue his genetics work while complementing his research activities with 'educational experimentation'.

Little's work as a university president introduced him to the elites of Detroit and Bar Harbor, Maine. His growing contacts with individual and institutional patrons such as the Rockefeller Foundation, but particularly Roscoe B. Jackson (whom Little met at Bar Harbor), help explain Little's challenges and also his successes as an organizer and institution builder. Jackson was a founder of the Hudson Motor Car Company of Detroit. He was in a financial position to support Little's summer field course in Bar Harbor (p. 66) and eventually to bankroll the eponymous laboratory. Little's struggle to gain institutional backing depended on convincing patrons like Jackson of the general scientific significance and public health value of linking genetics work with the popular public cause of curing cancer. Laboratory systems using mice (and a few other mammals) would link genetics with human biology. An emphasis on rigorous and systematic experimental evidence, which could only be produced from inbreeding practices like his own, would make Little's inbred mice standards for mammalian laboratory research. To Little, linking basic genetics and public goods such as cancer research (and eugenics) with a plan to deliver standardized inbred mice in quantity to the scientific community was the proper way forward. Such arguments to patrons and scientists alike paved the way for Little's move to Maine and the founding of the Jackson Laboratory.

Roscoe Jackson helped Little raise funds for his mouse laboratory among wealthy automaker friends, for example Edsel Ford, during their summers in Bar Harbor, Maine. Little was preparing to leave Michigan in frustration over his lack of success in research and faculty opposition to his educational reform proposals. Two events were pivotal in the founding of the lab, both of them financial. First, Roscoe Jackson died of flu in 1929, and although his widow and Detroit friends supported Little's move to Bar Harbor to construct a small, independent laboratory for mammalian genetics and cancer research, he had lost a key ally and patron. Second, the stock market crash of 1929 occurred on the eve of the lab's opening (p. 96). The Great Depression severely reduced the private wealth available for scientific philanthropy at the moment that flu carried off Little's most effective private patron.

Little travelled a rocky road to financial stability. Rader's narrative focuses on a surprising symmetry of the contingencies of Little's journey: the very same travails of funding explain both his successes and his failures in building and maintaining the laboratory, in cancer research, and in entrenching 'JAX mice' as laboratory standards. By 1932, private funding for the Jackson Laboratory had run out and renewed support was not forthcoming

due to the depression. The lab had focused on launching its research programs on the genetics of spontaneous tumors in inbred mice in these early years, but financial distress compelled Little to accept a US Public Health Service contract to provide it with mice in order to keep the laboratory going (p. 100). Economic pressure rather than research productivity drove the redistribution of resources toward scaled-up animal production, Rader argues, in contrast to the Morgan school's fruit fly program, (see Kohler 1994). Scaling up did not impel Little toward a *commercial* model of animal production, however. He favored traditional, cooperative exchange of materials as a service to the community of researchers. Indeed, many mice were shipped free of charge, even as the depression deepened and his funding dried up. Later, when the Lab was sued over its tax exempt status, Little defended its practices on grounds that they certainly could have made money as a commercial operation, but did not.

Rader's argument is that economic necessity was the contingency driving Little toward the notion that producing mice for sale could be more than 'mere animal caretaking work' (p. 114). Entering an agreement with Howard Andervont and J. W. Schereschewsky at the US Public Health Service to buy Jackson mice for their cancer research seemed to Little like selling out his scientific ideal of free exchange of research material, not a commercial opportunity as it would have appeared to a businessman of science like Henry Ward of Ward's Natural Science Establishment (Ward, 1948). At times, Rader's story reads like a B-movie in which impending disaster seems evident to all but the central protagonist. Little could have turned to mouse production as a commercial venture—that was what his laboratory seemed good at, so what held him back? What made the research ideal sufficiently powerful to steer Little in ways that frustrated his own success time and again? While Rader's narrative captures Little's story, and the story of the Jackson Lab, a full portrait of what made Little tick is not on offer in this book or indeed in this biographical genre of laboratory organisms.

Selling the number and quality of mice required by the PHS contract was critical to the transformation of Jackson mice into a *standard* of purity. Mice were to come from a specified tumor stock and be raised in the same environment as the parental stock (p. 120). The sales contract thus required a level of specificity and quantification in the exchange of material absent from the informal and smaller scale exchanges with individual scientists. Coupled with Little's argument that only Jackson could implement the controlled husbandry conditions required, the PHS contract entrenched Jackson's procedures in PHS research protocols and created opportunities and incentives for economies of scale and 'powerful imperatives for embracing businesslike values of efficiency and organization' (p. 123).

The decision to make mice available to the PHS generated demand that compelled scaling up. This then changed the focus of production to the development of standards. Notice that these were standards of purity, quality, and continuity, not standardized *mice* in the conventional sense in the research community that a particular strain was best and most desirable for research. Standardization, in other words, concerns the *substitutability* of mouse 'products' in a research consumer's usage. That is, standardization is about what happens when one 'plugs in' a purified, specialized mouse into a research process (experiment, breeding program). If one such mouse is *substitutable* for another, then the mouse meets a standard of purity. If husbandry practices and breeding protocols yield mice meeting particular standards of genetic purity, then one might also consider the practices and protocols to be standards as well. The promulgation of such a standard throughout a

research community (research market), depends on the substitutability of mice within a given research project.

The capacity to supply such standardized mice reliably on a large scale (i.e. to multiple research programs) requires a kind of industrial organization different from, if complementary to, the production of specialized pure strains for particular research programs. In 1937, a printed listing of mouse stocks included six different popular strains, and also their value for various kinds of scientific work. Articulation of genetic nomenclature for the varied mouse strains Jackson was producing, together with PHS notation for tumor types, served to standardize strain names, even though they arose from a highly contingent (and, Little thought, temporary) funding arrangement (p. 127). Rader quotes Little's application to the Rockefeller Foundation, emphasizing that 'material produced under standardized conditions will eliminate variables and make more practicable comparison or repetition of work in or between different laboratories' (p. 163). The *conditions* are standardized and rendered repeatable, while the *materials* are purified and specialized (by inbreeding) to take on particular value for specified kinds of work such as 'general laboratory work', 'genetic research', 'breast and internal tumor incidence'. The *Mouse Newsletter*, edited by Jackson scientist George Snell, served to standardize experimental *nomenclature* as it advertised the producers of inbred strains from many sources besides JAX, but also emphasizing that only JAX had them all (p. 170). And in 1941, 'JAX Mice' were registered with the US Patent Office. Thus, JAX mice became a standard in the context of a system of standardized practices and procedures for producing, distributing, and caring for inbred mice.

Moreover, the difficulties of maintaining husbandry conditions at the *receiving* end led Little to regiment mouse food, laboratory protocols (in a manual), and wooden shipping boxes. That is, in order for research consumers to produce stable, reliable, and repeatable results, their husbandry practices had to be standardized as well. Just as VCR or DVD ± RW standards for recording media are worthless if consumers lack equipment that can read them, genetic purity in a specialized JAX mouse is worthless if researchers cannot achieve phenotypic performance of husbanded mice comparable to those advertised by the Jackson Laboratory. As the depression deepened, Little continued to promote the value of Jackson Laboratory research in the search for a cancer cure. But by 1937, Jackson Lab was providing more mice for other and diverse research needs than it had to the PHS (p. 133).

It's important to note that the mice themselves became standards only with respect to specialized lines of work calling for particular inbred strains. Rader's conclusion, that 'The construction of a reliable mechanism through which researchers could obtain and use inbred mice helped transform the inbred mouse into a standard animal, both in terms of it being "widely available" and "widely used" ' (p. 174), elides the role of particular inbred strains. The mechanism producing 'the inbred mouse' resulted first in a standard of purity, while the particular strains are of value because they are *specialized* for different kinds of study. The mice of each strain are standardized, that is, substitutable for a given project; the different strains are specialized. Mice from one strain are, in general, not substitutable for those from another strain. Specialization and standardization trade off against one another to some extent; a strain tuned precisely to the need of a particular research program will not be suitable for a wide variety of programs even though they are produced by the same industrialized methods of breeding and husbandry.

One of Rader's more interesting arguments concerns the rationalization of research in the early twentieth century, which broadly reorganized around analytic problems (such as heredity, development, and geographical distribution) rather than taxon characteristics (Gerson, 1998). One became a transmission geneticist rather than a botanist, entomologist, or mammalogist. Rader focuses her attention to rationalization on the changing funding context from individual patrons such as Jackson, to private bureaucracies, such as the Rockefeller foundations. The concerns of the latter spanned many lines of work and soon came to promote the virtues of coordination and consistency (Kohler, 1991). The shift to public funding that began in the 1930s accelerated this tendency. The law creating the National Cancer Institute in 1937, for example, provided a new constituency and organizational impetus to Little's pursuit of the inbred mouse as a standard research tool. This was critical to the Jackson Lab financially since Little's attempts to gain substantial support from the Rockefeller Foundation had mixed success: the RF only seemed interested in supporting 'retail' mouse production for small scale mammalian genetics at Jackson, in contrast to the 'wholesale' fly program it supported at CalTech (p. 145).

Little's connection of mouse genetics to cancer was opportune but risky, as public demand for a cure rose alongside a movement against animal experimentation. The balance of interests tipped toward biomedicine and against experimentation in the case of rodents, however. Little's rhetoric shifted the Laboratory's focus from research more squarely onto standardization: mice as interchangeable parts, mice as 'chemically pure animals', standardized mice serving the democratic ideal of accountability to scientific peers. A key turning point detailed by Rader was the decision by the Surgeon General's National Advisory Cancer Council to support a National Cancer Institute grant to the Jackson Lab in 1937, through which 'the organizational suitability of inbred mice for experimental cancer research became official federal policy' and JAX mice a de facto 'industry standard', since the Jackson Lab was the only large scale provider until after World War II (p. 160).

One major argument of the book seems best summed up on pages 175–180. There, Rader observes that Little's dedication to a genetic explanation of cancer prevented him from taking the research steps necessary to explore alternatives, for example, viral or other acquired causes of cancer, in part because he felt discovery of non-genetic explanations might undermine the argument for JAX mice as genetically pure reagents for cancer research. Differently put, Little's argument for genetic research into cancer led to taking on the project of purification and standardization, and as the institutional arrangements were put in place to achieve those goals, they supplanted cancer as the primary reason a genetic approach was required.

Patrons, however, supported the Jackson Lab's research primarily as an indirect means of promoting the supply of JAX mice as standard laboratory tools or purified reagents and repeatedly withdrew funding of this precariously justified cancer research. Each time Little had to scramble for renewed financial support, the JAX standards for mouse breeding and husbandry ratcheted up and became more entrenched. Philosophers of science have rightly argued that the pursuit of 'false models' can lead to 'truer theories' (Wimsatt, 1987). Perhaps Little's story is one of unintentionally discovering that false models—his genetic model of cancer—can also lead to truer research standards. Each time the financial plug was pulled from Little's vision of inbred mice as a genetically purified standard for cancer research, he gained knowledge of how to entrench the mouse standard a little deeper, even if it meant a shifting array of audiences, allies, and markets for his mice: geneticists, tumor researchers, chemotherapists, and radiation biologists.

Mouse production increased more than tenfold from the 1930s through World War II. By 1947, Little was again making the case to the Rockefeller Foundation for support, but the argument had fully shifted away from research: Little's latest request was to fund buildings to house mouse production. Little contrasted the 'simple and quiet surroundings where resources are concentrated on a single objective and the complex and confused environments of great universities where competitive interests . . . continually arise' (p. 207). As a locus of material production for research, the Jackson Laboratory made a uniquely valuable contribution. Rockefeller granted the funds.

On 23 October 1947, a fire killed fourteen people and tens of thousands of mice, destroyed the original laboratory, and damaged two of the new 'mouse houses' (p. 1). Economic contingencies, once again, were pivotal for Little and the Lab. The fire drew national attention to the Lab, giving huge publicity to its mice and their role in biomedical research, and completing the transformation of Jackson Laboratory into a production facility rather than a research organization, the center of a materials network rather than a 'center of calculation' (Latour 1987). Mouse stocks were rebuilt after the fire, in part, through gifts of breeding pairs of mice sent back to JAX by individual researchers. At the same time, the obsolescence of Little's 'paternalist' pre-war managerial style (p. 215) became evident as the rebuilt laboratory became fully the 'bureau of mouse standards' the Rockefeller Foundation thought it to be (p. 216).

In the 1950s, JAX standards became commercialized when cancer therapeutic drug development came under the coordination of the federal Cancer Chemotherapy National Service Center. The demand for mice to be used in screening led to outsourcing of mouse production to commercial suppliers following JAX inbreeding protocols. A final post-war development described by Rader in *Making mice* was the advent of radiation biology. The study of induced mutations and radiation risk became big research business and mice became key test organisms for radiation genetics. The 'mega-mouse project' of Liane and Willliam Russell (a former JAX researcher and student of Sewall Wright) at Oak Ridge National Laboratories in Tennessee attempted to produce and measure mutation rates due to ionizing radiation. This 'mission oriented' biomedical research under the aegis of the Atomic Energy Commission and organized on the model of the Manhattan Project relied on a particular specialized mouse strain, SLT. The scale of the mega-mouse project virtually guaranteed that SLT would become a mouse standard for mutation studies and, in conjunction with the scale up of federal research on radiation, ensure that Jackson Laboratory standards for inbred mice would become deeply entrenched in American biomedical research.

3. Historiography of standardization in science

Although *Making mice* is not strictly a biography of Little, his organizational drive, entrepreneurial spirit, business acumen, and social network are key to Rader's description of Little's surprisingly rapid career trajectory over a decade. Rader identifies a fundamental shift in support for scientific research in America at this time, from small individual grants to 'programmatic funding for cooperative discipline-building' (p. 61). She also details Little's need to scale up his mouse breeding operations during the period of his university presidencies in order to stabilize them from the threat of epidemics or chance losses in transit.

The scaling up problem focuses attention on the story of mouse standardization in a different way from other organism biographies. Her project is not so much a shift of

attention from scientist to model organism as an entwining of the careers of scientist, laboratory, and mouse. Rader's narrative offers an historiographic counterpoint to the recent spate of organism biographies of rats (Clause, 1993), corn (Kimmelman, 1992), flies (Kohler, 1994), nematodes (Ankeny, 1997), and viruses (Creager, 2002). In these, Rader argues, scientists appear to quick march under the banner of efficient, productive model organisms and Taylorized laboratory systems straight to the heart of core problems of twentieth-century theoretical and applied biology. Rader takes these narratives to assume that standardization of organisms in combination with universal scientific norms is prerequisite to the success of rationalized modern science. Instead, she argues that such standards are consequences rather than causes of scientific consensus (p. 15). She notes that in experimental biology, the material and practical aspects of standardization are 'synchronic', so a nuanced story of local and highly contingent institutional and organizational arrangements is needed to account for the emergence of standardized organisms.

Rader's project addresses a paradox of Little's role in the biographies of the mouse and the Jackson Lab 'mouse house'. Although genetically specialized inbred JAX mice became the 'gold standard' of biomedical research by mid-century and the laboratory became the 'National Bureau of Mouse Standards', the research projects for which Little promoted the mouse model and with which his laboratory pursued a genetic model of mammalian cancer were not particularly successful, raising questions about the historical alignment of scientific research with discipline and institution building. 'In other words', Rader writes, '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?' (p. 17).

Rader's solution begins by noting the connection between medieval and early modern meanings of 'standard'. The latter and now common meaning of 'an object or quality that serves as the authorized basis or principle to which others conform or by which they are judged' (p. 16), must be complemented, she argues, with an older notion of a standard originating in warfare: 'a conspicuous object, such as a banner, carried at the top of a pole and used to mark a rallying point' (p. 17). Rallying biomedical science around genetically pure mice in order to pursue problems of cancer biology was Little's institutional goal. His cartoon representations of the mouse for scientists and the public (illustrated throughout the book) include an effort to initiate a joint 25th anniversary celebration with that other famous rodent, Mickey Mouse. Such efforts testify to Little's use of the mouse as a rallying standard bearer. However, his success as an entrepreneur and cheerleader, aided by connections with elite patrons developed during his days as a university president, was complemented by failure as a cancer geneticist. Rader's achievement is to draw attention to the need to follow both aspects in telling the story of the standardization of the laboratory mouse. Had Little succeeded as a researcher, his mouse standardization enterprise might well have failed.

Rader plots contours to make a topographic map of Little's scientific campaign, putting the analyst of science in a better position to interpret the contingent elevations and local depressions of scientific work in the broadest sense as at once laboratory practice, organization building, and alliance formation. This approach appeals because linear narratives of the march of scientific progress along predefined roads mapped out by universal scientific norms of improved precision, accuracy, objectivity, and truth are clearly not up to the task of analyzing a history of standardization. Traditional biography offers few resources

for a contextually aware science studies. In that sense, Rader's book is a success. In the course of mapping the terrain, however, Rader offers scant comparative interpretation of her data to advance beyond the historiographic traditions she criticizes, despite her ambitious introductory chapter laying out historiographic and analytical goals. The epilogue draws together elements of her chosen landscape into a much needed inventory, but far from an effective analytical model. This lacuna is not unexpected because the value of Rader's historical data for science studies lies ultimately in a fully comparative social analysis, which would have doubled the book's size and changed its analytical focus from biography—of a man, an organization, and a model organism—to sociology of science. Thus, we can applaud Rader's historical data and historiographic turn and at the same time wish for a more developed assessment of their significance.

'To understand how broader cultural imperatives shaped the practical nature of standardization in research, and vice versa' (p. 7), the local contingencies and alliances in Little's scrappy, entrepreneurial struggle to keep the Jackson Lab alive must be evaluated and weighed against other stories only cited or briefly mentioned by Rader, with different circumstances and contexts. Rader explores in detail the ways in which the mass production of specialized mice became a financial imperative for the Jackson Lab and thus the proverbial tail wagging Little's dogged and marginally successful pursuit of the genetic basis of cancer. The Great Depression, the shifting priorities of the Rockefeller Foundation, relations with medical school researchers, the founding of the National Cancer Institute with its various mandates for biomedical research—all these are critical features in the landscape Rader maps.

At the same time, we need to understand in rich detail the laboratory projects and practices of Little and his colleagues and how they were transformed by Little's use of the mouse as a standard bearer for his genetic model of cancer. We learn from Rader that the mouse became standardized because it was used as a standard bearer, but not exactly what a standard mouse 'looks' like, precisely what it is to be standardized (in the sense of substitutable), or what the evidence is that the mouse truly is standardized, rather than merely common across the several disciplinary specialties in which Little and his colleagues worked. Rader's evidence shows that JAX mice spread, but without evaluation of other sources and patterns of contemporary mouse production and use, the social place and economic position of JAX mice remains uncertain. By analogy, learning that Apple Computer grew to become a multibillion dollar company over twenty years has one meaning, but learning that its market share declined by an order of magnitude over the same period has a different meaning.

For example, in Chapter 5, Rader points out that by 1947, JAX inbred mice were not universally used, 'but JAX's distribution network and product recognition had generated a reliable constituency, especially in cancer research' (p. 181). This shows that JAX mice were specialized and frequently used, but not that they constituted a *standard* for laboratory mice. Her quantitative data tell the same story: use of inbred mice rose from less than one percent of studies in the journal *Cancer Research* in 1932 to over thirty percent in 1937 to about seventy percent in 1947 (pp. 181–182). However, the market *share* of JAX mice is unknown. (Rader notes that Jackson Lab was not unique in its mouse breeding goals, even at the time the lab was set up, p. 99.) Whether the important story is JAX product placement or rather the spread of inbreeding as a standardized *protocol* instead of a JAX mouse standardized *reagent* requires more extensive comparative analysis.

If '[e]xisting narratives beg larger questions about the underlying values motivating the process of adopting standardized animals and other model systems at the bench-top' (p. 15), Rader's narrative leaves unclear how the bench-top protocols and practices Little developed out of classical husbandry practices and classical genetic techniques *articulate* with projects and problems of standard bearing and concepts of standardization in the various social worlds in which Little and JAX participated. Rader need not be faulted. She has taken great pains to reconstruct JAX's financial vicissitudes, which is central to the problem of articulating Little's entrepreneurship with mouse standardization. But at the same time, it is harder to understand from Rader's account *why* Little's program for mammalian cancer research at Jackson Lab failed to sustain that institution than, for example, from Kohler's account, why Morgan's fly lab transmission genetics and linkage mapping program became a self-sustaining 'breeder reactor' (Kohler, 1994). Or indeed why Little seems to have had such a difficult time accepting or even recognizing that the research line he took *was* unsuccessful and that his dogged pursuit of a marginal line of work was fundamentally unsustainable in the context of a private, non-profit research institution rather than a university, industrial, or government agency laboratory. Or, perhaps that *is* the story: maybe only an entrepreneur with a vision powerful enough to mask his scientific inadequacy could keep a marginal institution alive long enough to become entrenched as a standard bearer and standards producer in the face of a failing scientific program and a worse business plan.

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