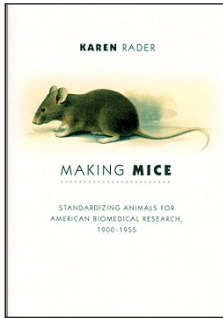


The mouse house



Making Mice: Standardizing Animals for American Biomedical Research, 1900–1955

By Karen A Rader

Princeton University Press, 2004

312 pp. hardcover, \$45

ISBN 0-691-01636-4

Reviewed by Alan Packer

This book begins with a terrible fire. On 23 October 1947, much of the resort community of Bar Harbor, Maine burned to the ground. The entire population was safely evacuated, except for 14 people who died along with 90,000 laboratory mice that had been housed in a building at the Jackson Laboratory, a then-18-year-old center for research on mammalian genetics and cancer that was known to only a few.

And then a remarkable thing happened. Within days, public and private institutions, including the US National Institute of Health and the Rockefeller Institute for Medical Research, pledged financial help to rebuild the lab. What's more, researchers from around the country sent back breeding pairs of mice that they had received from the lab, in an effort to restore the collection of inbred strains that had been painstakingly assembled over the previous two decades. The story of how (and why) the 'Great Bar Harbor fire' led to such a determined response is told in Karen Rader's interesting and valuable book on the rise of the laboratory mouse as a model organism for research in the US.

Making Mice is, to a large extent, the story of Clarence Cook Little and his effort to establish standardized inbred mouse lines as essential resources in the study of genetics and cancer. Although the reasons why inbred mice are useful seem obvious now, Rader makes it clear that Little's was a somewhat lonely voice. Mentored by Harvard's William Castle, Little was one of a handful of researchers who drew on the expertise and enthusiasm of amateur mouse fanciers. These hobbyists, who had been producing large numbers of coat color mutants, would provide the material for the kind of systematic breeding program that Castle, Little and a few others envisioned.

Rader points out that Little's enthusiasm for inbred mice as a research tool derived from a combination of factors. The first was simply proximity: "...the fact that Dr. Castle left me alone with a large number of mice and that the mice themselves provided a sufficient number of unknown factors to become interesting". More importantly, mice that showed differential susceptibility to tumor formation became an obvious research tool with which to study cancer—especially inbred mice, which Little argued constituted "an

effective way to weed out variation and preserve a unique variant against a homogeneous genetic background".

Armed with this conviction and a growing collection of mice, Little spent the years after obtaining his doctorate in 1913 at Harvard's Bussey Institution and at the Cold Spring Harbor Laboratory, ultimately rising to the presidencies of the Universities of Maine and Michigan. Although Little's plans for mouse research progressed and he was highly regarded in Ann Arbor, a protracted conflict with the Michigan regents and trustees over his proposals for educational reform led him to resign the presidency early in 1929.

Fortunately, he had benefactors. A group of Detroit industrialists, including Hudson Motor Car Company president Roscoe B. Jackson, supported Little's idea of building an institute on Mount Desert Island, Maine—a permanent home for these inbred mice and a center for research on mammalian genetics and cancer. When Jackson died of influenza as construction was set to begin, Little and his patrons decided to name the laboratory after him, and work in the Jackson Memorial Laboratory began almost exactly 75 years ago, in November 1929.

That particular November, only weeks after the stock market crash, was not a good time to launch a new venture that relied on private capital. Thus, Rader sets out, in the middle section of her book, to explore the tension between science and commerce, which is exemplified by Little's efforts over the next two decades to keep the Jackson Lab afloat without compromising its claim to being a center for innovative science. As his efforts to promote the usefulness of inbred mice in research took hold, Little is portrayed again and again as stubborn in his insistence that the lab was not to be reduced to the status of a mouse store. Eventually, increased demand for the mice, financial need at the lab and the realization that he was sitting on a gold mine made the decision easier, and 'JAX' mice were soon being mass-produced and sent to institutions all over the country. Thus, the Jackson Lab survived the Great Depression, and the number of publications reporting the use of inbred strains, particularly in cancer journals, soared. By the mid-1950s, when the US Congress set aside \$70 million to test cancer therapeutics in inbred mice, JAX mice were indispensable.

Although Rader includes an interesting chapter on the work of William Russell and Liane Brauch Russell in establishing the Oak Ridge National Laboratory as a center for the study of radiation risk in mice through their 'Specific Locus Test,' the book's narrative is sustained by the story of C.C. Little and his stewardship of the Jackson Lab. It is written for an academic audience and as a result, the style is occasionally dry. That said, Rader is alert to the human interest in Little's earnestness, noting his quixotic (and ultimately failed) attempt in 1953 to convince Walt Disney to create a film that would celebrate the upcoming 25th anniversaries of the Jackson Lab and Mickey Mouse. Some things are better left to the imagination.

On pages 921 and 925 of this issue, two commentaries present the consensus of leaders in the mouse genetics community that the time is right for a concerted effort to mutate every gene in the mouse genome and to make these mice widely available. If you want to know how the laboratory mouse came to have such a central role in modern biomedical research, *Making Mice* would be a good place to start. ■

Alan Packer is Senior Editor at Nature Genetics.