

standards have driven up the purchase cost of materials by 8 to 10 percent and doubled the cost of some equipment.

These added expenses—combined with the general inflation in the cost of doing research during the 1960's and on into the 70's—dealt a harsh blow to reactor safety research. As

costs rose, the program's overall budget grew slowly in some years and remained static in others. At the same time, the Atomic Energy Commission, partly in response to prodding from the Joint Committee on Atomic Energy, found itself accelerating the breeder program, and dipping into money al-

located to water reactor safety to do it. Something had to give, and what gave was research intended to resolve questions of the utmost urgency pertaining to dozens of commercial nuclear power plants then on the drawing boards and under construction.

—ROBERT GILLETTE

## The Jackson Laboratory: "Mice Are Our Most Important Product"

The Jackson Laboratory is a mouse house. Nine months of the year—especially in the icy dead of a Maine winter—the laboratory perks steadily along, in a remote, self-contained world in which a small band of only 34 scientists and their mice pursue the business of biological research. Investigators delve into questions ranging from reproductive physiology to aging, from cancer and transplantation immunology to behavior and environmental stress. It is a place where a person can work in an atmosphere of comparative calm, where people innately take the long view, where one can presume to stick with a single research problem for years, even decades, if need be.

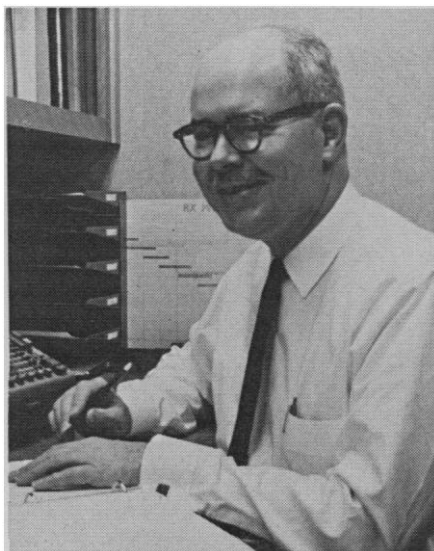
With the coming of spring, the laboratory gets ready to assume its summer personality, and from June to September the isolation is broken by the arrival of visiting scientists and students, who come to take advantage of the three attractions that this institution alone can offer: (i) millions of mice, each carefully bred; (ii) ready access to the impressive expertise of those 34 researchers, who, collectively, probably know more about mice than anybody else; and (iii) the pleasures of a summer on the coast of Maine. During those months, which laboratory scientists quaintly refer to as "our busy time," the scientific population more than doubles.

Situated just 3 miles south of Bar Harbor on Mount Desert Island, the Jackson Laboratory has summer appeal that simply cannot be matched, especially if you have a taste for lobster or ocean sailing and happen to be a scientist with a fancy for genetics. Earl L. Green, who has been director of the

laboratory for 16 years, says proudly, "It is the only private, nonprofit research institution devoted to mammalian genetics in the world." Then, as if to put that in perspective, he adds, "Of course, the world needs only one."

Assessing their public image, most staffers placidly concede that, as one of them put it, "Half the scientific world doesn't even know we exist"; yet they clearly thrive on the knowledge that the Jackson Laboratory is Mecca to anyone tuned in to mammalian genetics. And they take satisfaction in knowing that mammalian genetics is steadily gaining importance as a scientific discipline. "This is a golden time for mouse genetics," Elizabeth (Tibby) Russell, a laboratory geneticist since 1937, says fondly, with a measure of gratification that anyone might feel on watching the object of her life-long interest achieve new prominence.

For years, mouse geneticists have been



Earl Green

a group unto themselves, a cadre of workers who each knows the other and shares his extraordinary enthusiasm at the discovery of a new gene mutation in a mouse. Many investigators in the larger, richer fields of science think of mouse geneticists as a pleasantly eccentric bunch. Some human geneticists have, at times, looked down their noses at the devotees of the mouse as being amateurs.

But now, mouse genetics is coming into its own. "The point to make about the Jackson Laboratory," says Park Gerald, a geneticist at Boston's Children's Hospital, "is that it is growing in importance. The lab is on the ascendant, becoming significant in its own right as a research center and not just as a supplier of mice, invaluable though that is." Gerald has been a frequent summer visitor to the laboratory.

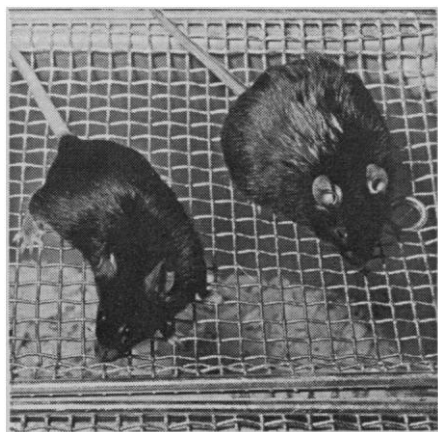
During the last couple of years, in part to the credit of Jackson scientists, there has been remarkable progress in deciphering the genetic makeup of the mouse. New techniques in chromosome identification—chromosome banding techniques—have emerged that enable investigators to spot individual mouse chromosomes with a degree of precision that was previously impossible. Because mouse chromosomes look so much alike, standard karyotyping techniques that have been useful in looking at the gross structure of human chromosomes have not been terribly valuable to mammalian geneticists. Now, armed with banding techniques that distinguish finer points of structure, many gene linkage groups already have been assigned to specific locations on mouse chromosomes. "It will now be possible to extrapolate data from mice to man," says Gerald. The gap between mammalian and human geneticists is closing and people on both sides seem eager to get on with some collaboration.

The laboratory, as Earl Green sees it, exists to conduct research, train students, and grow mice. It is in its latter capacity that the laboratory is best

known, and, in both a literal and a metaphorical sense, staff members are right when they say, "Mice are our most important product." Last year, they sold 1,621,915 highly specialized, genetically defined inbred, hybrid, and mutant mice to investigators in the United States and abroad. That gained them about half a million dollars to plow back into the laboratory. They used nearly 1 million mice themselves.

JAX mice, as they are known, come in about 100 inbred varieties and a range of prices. For 75 cents you can buy a hybrid that is technically identified as a B6D2F<sub>1</sub>/J (C57BL/6J ♀ × DBA/2J ♂). Its mother was what is commonly called a C57 black, its father a DBA. At the other end of the financial spectrum, a breeding pair of diabetic mice would set you back \$18. These animals are expensive because they're not very good at breeding, which means that maintaining the line is a taxing proposition. The inbreeding that keeps diabetic mice coming through the production lines reduces their reproductive capacity (not the case with the majority of inbred strains). Therefore, at times the strain must be kept going through delicate and time-consuming surgery, in which the ovaries of diabetics are transplanted to normal females. Anemic mice sell for between \$6 and \$12 a pair, a quaking mouse costs \$9.50 or \$15 for a breeding pair. A set of hairless mice are \$6. Because of the President's new price guidelines, no increases are anticipated.

JAX mice are bred to rigid genetic standards in a one-story brick edifice in which sterility is of the essence. Infectious organisms that could spread disease which might wipe out the mouse colonies or induce uncontrolled mutations in the precious stock are feared beyond words. The breeding house, with its precisely regulated air pressures,



A diabetic mouse (right) grows fatter than his normal cousin.



Elizabeth Russell

autoclaves for sterilizing food, mouse pens, and bedding, and animal caretakers who handle their charges only with disinfected forceps, operates under all of the strictures one associates with places like Fort Detrick, a former chemical and biological warfare laboratory now being converted for the study of cancer viruses.

Although gaining admission to the research laboratories is a less dramatic procedure than getting into the breeding house, which requires a change into sterilized overalls and plastic boots, visitors are not free to wander around the laboratories at will. No one who has been around laboratory animals during the 10 days before coming to Bar Harbor is allowed past the public rooms. The regulation is strictly enforced by laboratory staffers at all levels. You cannot go anywhere without a badge, and, even with one, you will be directed around buildings rather than through interior corridors by anyone who is not sure whether it is all right to let you in. No one takes the matter lightly.

Since its founding in 1929 when Clarence Cook Little convinced Hudson motorcar magnate Roscoe B. Jackson and other wealthy Bar Harborites to help him found a laboratory for the study of cancer using inbred mice, there has never been an epidemic. The precious mouse stocks were virtually wiped out once, however, during the fall of 1947, the time of the famous fire. Today, the fire of '47 is almost a legend on the island, probably the single most dramatic event to have oc-

curred in this century. Islanders are fond of telling the tale which was described in a memorial tribute to Little thusly: A fire started in a dump northwest of Bar Harbor and raged out of control for 3 days, driven by a southerly wind. On the afternoon of 23 October, the wind died for a few minutes and then suddenly roared out of the northwest. The fire, turned by the 60-mile-an-hour gale, erupted into a giant blowtorch and charged toward Bar Harbor. Nearly 2000 men equipped with modern equipment stopped the fire at the edge of town but it swept unchecked to the southeast. The flames destroyed the Jackson Laboratory in minutes.

Grateful scientists throughout the world who had received stocks of mice from the laboratory promptly sent back breeding animals to restore the colonies, the publicity put the laboratory on the map, and everyone gamely started over.

New buildings now nearing completion should eliminate some of the problems about what to do with possibly contaminated guests who could be as dangerous as fire. A year and a half ago, the laboratory launched a \$1.6-million construction project for a new mammalian genetics laboratory and a library-conference center. "The laboratory," says Green, "will house 60,000 mice in eight rooms designed to provide the best possible environmental protection." Thus, the walls and floors of the new animal quarters will be impervious to air, water, and detergents. Light-dark cycles will be independently controlled in each room, as will air supply systems for the regulation of temperature and humidity. Air



The hairless mouse and its genetically identical cousin—except that it has hair—contain leukemia viruses. At a comparable age, the hairless mouse strain has a 50 to 75 percent incidence of leukemia; the strain with hair, only a 1 to 2 percent incidence. Now, investigators are tracking down the gene for hairlessness which reduces resistance to this cancer.

pressure systems will be designed to thwart airborne microorganisms that might otherwise gain entry to the animal rooms.

To all of these precautions has been added one other, to everyone's apparent relief. Visitors will no longer have to go near the research laboratories in order to get into the library or meeting rooms, thereby further reducing the chances that the mouse colony will be exposed to any infectious disease. The library will hold 20,000 volumes, the new auditorium, 124 people. A conference room will have 30 seats. It gives one a sense of the scale of things at the Jackson Laboratory. Its small size is, of course, a predominant feature of the place, essential to maintain-

ing the family atmosphere that devotees of the laboratory find so appealing. It is also, some family members think, a disadvantage. A number of scientists intimately familiar with the laboratory have called it "parochial in many ways." But a family it is, and you have to be a special sort of person to fit comfortably into the laboratory and the landscape. People who fit, who like the intimacy of the laboratory and don't mind being isolated most of the year, usually stay a long time.

"The setting tends to bring out feelings of devotion in the people who work here," observes Green, who is repeatedly described as being a cool, smooth, efficient director, somewhat aloof, a person of formal dignity. He

calls his staffers self-sufficient types, people who can generate their own entertainment and thrive on the companionship of only a few close friends. Those who are frustrated by the island's conspicuous lack of theaters, nightclubs, and posh eating places, who enjoy frequent parties and the like, usually depart after a year or two. Although he withdraws the word after using it, for fear of its pejorative connotations, Green thinks there is a bit of the "recluse" in each of the members of his "laboratory family." "Yes," he says reflectively, "that applies to everyone, everyone except Tibby."

Tibby Russell, 59 years old and the mother of four grown children, is generally regarded by her admiring col-

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## New Levich Statement Deplores Campaign against Him

Scientists from many countries attended the Fourth International Biophysics Conference in Moscow from 7 to 14 August, but some of the activity during the meeting centered around someone who was not there: Veniamin G. Levich. An electrochemist, Levich has had his application for an exit visa to Israel denied. He has lost one of his jobs and been demoted in the other; his books and scientific papers have been removed from circulation in Russia; even citations of his work in the scientific literature have been deleted. Levich is a corresponding member of the Soviet Academy of Sciences and the most prominent Russian scientist to suffer the harassment which appears to characterize treatment of some Russians attempting to go to Israel. *Science* has obtained a copy of a hand-written statement in which Levich protests his being barred from the Biophysics Conference and appeals to the world scientific community for help. Of the debarment Levich says:

... The reason is quite obvious. The scientists who apply to the authorities for the permission to leave for Israel are magically transformed into outcasts who are deprived of any right of continuing a scientific activity: publications forbidden, lecturing forbidden, making scientific reports forbidden, even being cited forbidden.

A person is immediately expelled from any kind of scientific councils, editorial boards, demoted, and often fully discharged.

A person is constantly living under the conditions of permanent pressure and

anguish for the fate of his family and himself. As is known, the Soviet government gives a permission for repatriation to many Jews, but [to] no scientists.

The violation of the civil rights of scientists as compared to other people and the transformation of scientists into the property of the Government is a dangerous precedent.

Today it is the fate of perhaps a small group of scientists at a certain place of the world. Tomorrow it may happen to anybody and anywhere.

The brains as well as the hands of any human being are his personal property.

I believe as well that the persecution of scientists and the prohibition of their scientific activity as a punishment for their moral and conscience convictions is inhuman, immoral, and disgraceful.

... The international scientific community, I believe, should not consider such problems as a personal affair of each of us, but as a problem of the professional honour, dignity, and humanism of all the scientists all over the world.

So far, the National Academy of Sciences has taken no public, official action on the Levich case, although it has been discussed in NAS Council meetings. At the moment, consideration is being given to a joint statement signed by several heads of national academies of sciences and addressed to the president of the Academy of Sciences of the U.S.S.R., M. V. Keldysh.

However, British scientists have been active: Sir Maurice Wilkins, Nobel biophysicist and president of the British Society for Social Responsibility in Science, has circulated a petition strongly protesting Levich's treatment

and other "recent attempts to harass Soviet scientists who disagree with officially accepted views." Also, D. B. Spalding, of the Department of Mechanical Engineering, Imperial College of Science and Technology, London, is circulating a petition calling on Soviet scientists "to abstain, if they can, from any further harassment of Professor Levich and his family." Sir Frederick Dainton has offered Levich a 1-year post at the Physical Chemistry Laboratory at Oxford.

A number of those attending the Moscow Biophysics meeting were able to visit with Levich and his family. One who did, Harold Scheraga of Cornell, had his luggage searched and his plane detained by 15 minutes at Kiev. Two National Institutes of Health researchers who saw Levich are Robert Adelstein and Jack Cohen. When Adelstein and Cohen visited with Levich, Levich drew them a graph which he said illustrated his present situation. The x-axis was labeled "time" and the y-axis was labeled "noise." Levich drew two curves on the graph; one rose above a certain "noise" level and was labeled "Israel." The other peaked below and was labeled "jail or death." Both Adelstein and Cohen, as well as others who have been in contact with Levich, agree that more public forms of "noise" could help Levich. It could also prevent the Soviet authorities from turning the Levich case into a symbol in order to discourage other Russian scientists from trying to emigrate.—D.S.

leagues as "the personality of the place." Last April she received what everyone associated with the Bar Harbor laboratory agrees is well-earned recognition when she was elected to the National Academy of Sciences. "Tibby leaped straight up out of her chair and shouted for joy when Earl told her," a friend recalls. Unabashedly pleased by her election and interested in participating actively in the work of the academy, she says that one of the reasons the honor so delighted her is that "Everybody writes you a nice congratulatory letter when you get in and that makes you feel good." She expresses some "disappointment," however, at the fact that only one other woman (physicist Gertrude Scharff-Goldhaber, of the Brookhaven National Laboratory) got in. "I'm not an active women's libber," says Russell, who looks a bit like everybody's favorite grandmother, "but I do think the academy should have more women."

Although the Jackson Laboratory has no such thing as the kind of star system that operates in university science enclaves ("This will never be a Caltech," Russell quips), it is people like Tibby Russell, immunogeneticist George Snell, and the late founder C. C. Little, all academy members, who have done so much to cap the laboratory's reputation as a place where solid, reliable work is done with a touch of prestige. Its impeccable, if less than glamorous, reputation within the biological community, combined with its vital service role as mouse supplier par excellence, seem to have kept the wolf from the door during the last few years of fiscal depression. Good management apparently helped too.

Green, who many of his associates find "difficult" to work with, and who has been criticized for lacking the spark and zest of his predecessor, is virtually unanimously acclaimed for his administrative acumen. "The laboratory is run like a ship," one observer comments appreciatively. "Earl really makes the place run smoothly."

In 1968, when it was apparent that federal research support was going down, laboratory scientists prepared to retrench, gritting their teeth to face painful cutbacks on the horizon. But disaster never struck. "We really have not been hurt very much at all," says Green, something one doesn't hear very often these days. A few staff scientists, "particularly a couple of younger ones," were so afraid of losing grants that they left for larger institutions, Green reports, "but in the end, the

cuts never really came." Not by a lot, anyway. In fiscal 1968, the laboratory's scientists garnered \$2,145,796.65 in research and training grants. In fiscal 1971, they got \$2,079,454.06 in grant funds, up a little from fiscal 1970, down a little from fiscal 1969.

To keep its research and mouse colonies going, the laboratory cut back to the extent of not conjuring up new and elaborate projects, dropping such social frills as laboratory-hosted cocktail parties at the prestigious Pot and Kettle Club whose members are the island's many millionaires, and switching funds from a general support grant from the National Institutes of Health. The laboratory had been using that \$175,000 grant to buy major pieces of equipment, support visiting scientists, and so on. "Now," says Green, "we use that money to back our core research program. It is just enough for us." He'd love to return to the days when that money could be spent on special projects, however, and hopes it may be coming. The rest of the laboratory's \$4-million budget comes from donations (which have remained stable at about \$100,000 for the last 5 years), the sale of mice and, on a small scale, rabbits, and such things as interest, and fees from its many training programs.

#### Training at Several Levels

The laboratory is geared for training high school and college students, as well as M.D.'s, Ph.D.'s, postdocs, and established investigators whose work brings them into the field of mammalian genetics. About 24 high school students come every summer—598 have come altogether since the program's inception in 1949—to learn about the day-to-day aspects of life in the laboratory. They are housed together at Highseas, a once elegant old mansion high above Frenchman Bay that has been converted to a dormitory and meeting center. There, they are looked after by a resident scientist and four counselors, in a setup characteristic of most boarding schools. College and graduate students live on the laboratory's campus in a cluster of low buildings that were built in the late 1940's and look it. Visiting scientists live scattered throughout the island with its chic, old-line towns such as Northeast Harbor and Seal Harbor. (Today, downtown Bar Harbor itself retains only touches of what is said to have been its former flavor; it has acquired all the accouterments of a mediocre tourist town.)

Visiting scientists come in two cate-

gories. There are those who arrive for a couple of weeks to attend special courses and meetings, such as the well-known short course in medical genetics which the laboratory cosponsors with the Johns Hopkins University and the support of the National Foundation. And, there are those who come to stay for the entire summer. To be a summer visitor, one must have a sponsor, a staff scientist who, as Green explains it, says to the guest, "I'll take care of you and give you space in my lab to work." Very homey, very friendly.

Kenneth Paigen of the Roswell Park Memorial Laboratory in Buffalo is a visiting scientist whose reasons for migrating north for the summer typify those of his other temporary colleagues. "The island," he says, "is such a nice place. And the mice and the available expertise give me something I cannot get any place else." Paigen is interested in the relation between single genes and enzyme activity during development. The laboratory, which makes its production facilities available to its guests, can offer him mice at all stages of development, handy, generally readily available, in numbers and varieties that would be prohibitively expensive in other circumstances. Besides, he notes, conversations with the staff help him move in directions he might not otherwise go, ask questions that might never arise if contact were restricted to long-distance phone calls. Paigen finds the Jackson Laboratory restores his interest, makes him "want to do science again. Psychically it is very good." No one would disagree.

In many ways, it is not just the setting but the singleness of purpose that makes the laboratory unique in itself and in its appeal to others. In spite of the fact that its staff is active in a number of different scientific areas, there is unity in the fact that each approaches his work through the eyes of a mouse geneticist. As Green says, "The entire laboratory is a specialized resource and everyone's single purpose is the exploitation of that resource—mice. We have no diverting responsibilities—no full-time teaching duties, no hospital to worry about, no football team." That singleness of purpose is, as many people see it, the laboratory's strength and that feature, which is now being described by some as its "mission-oriented" approach, may do much to keep it in the black. Looking ahead, Elizabeth Russell says, "I think we'll probably do very well in the new era."

—BARBARA J. CULLITON