Gerald Rubin

Photo by Paul Fetters

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You need to be careful about what you wish for and Gerry Rubin has been careful indeed. In 2002, the Howard Hughes Medical Institute (HHMI) gave Rubin the scientific equivalent of a magic lantern full of wishes: anything Rubin needed to create a breakthrough research institute. Late last year, the world got its first tentative look at what Rubin has been wishing for: Janelia Farm, the new HHMI interdisciplinary neurobiology and imaging research campus in suburban Northern Virginia.

Janelia represents an initial $500 million investment by HHMI in land, buildings, and people, and a subsequent, projected annual operating cost of $100 million. The site just south of the Potomac River in exploding suburban Northern Virginia covers 689 acres; only 60 are being developed currently. The central Landscape Building, at 317,000 square feet, is slightly larger than the nearby Dulles International Airport terminal. Designed by New York architect Rafael Viñoly, the lab building is a "green" architectural showcase. The S-shaped, triple-decker building was set edgewise into a river bluff and half-buried under the second-largest green roof in the U.S. Storm water and roof runoff are channeled into two artificial lakes. The landscaping is drought-resistant. Trees cut onsite during construction were 100% recycled into everything from garden mulch to random-width flooring for visitor housing. Daylight floods the lab building through its curving, north-facing glass wall and inset cell garden light wells. Technology and room for future technologies were built into everything.

Live at the Lab

Stunning as the lab building appears to visitors, it represents only the tip of Gerry Rubin's vision of what it takes to cultivate breakthrough science. Janelia is interdisciplinary, collaborative, and residential; some scientific staff and a number of scientific visitors, including lab director Rubin, and their families live in HHMI-provided housing on the grounds. The 24 group leaders are expected to be onsite at least 75% of the working year. Instead of jetting around the world to conferences, Janelia researchers will have the science world call on them for leading-edge workshops and conferences or for short-term, Janelia-supported (and housed) fellowships.

Janelia is focused on basic neurobiology and cutting-edge imaging technology and computational analysis needed to understand neuronal circuitry. Completely funded from HHMI's private coffers, Janelia is divorced from the vagaries and prejudices of the public funding system.

In designing Janelia, Rubin explains that he tried to draw on the best aspects of places he's worked such as the Medical Research Council (MRC) Laboratory for Molecular Biology in Cambridge, England (where Rubin did his Ph.D. work with Sydney Brenner) and the Cold Spring Harbor Laboratory (CSHL; where Rubin studied and did summer lab internships while an MIT undergraduate). He also was inspired by places that he'd admired from afar, like the famed AT&T Bell Labs in Murray Hill, NJ. (That's where the laser and other major inventions had their start.) Rubin jokingly describes himself as Janelia's "PI in a sociological experiment." Indeed, the result is not only an astounding laboratory building but a highly engineered social environment as well.

Small Science, Big Science

Janelia Farm is not without its critics. Some contend that the money could have been better spent on beefing up the number of more traditional HHMI Investigators at research institutions around the world. The critics are missing the point of Janelia, says Joan Ruderman of Harvard Medical School (HMS), because they don't understand the ambition behind it. "I wouldn't call Janelia an experiment but a new kind of institution that has tremendous potential. It's a very powerful melding of big and small science. The [lab] groups are limited in size to six, including the group leader who works at the bench, but this small science part is linked to big science with big leading-edge technological development and technical support. Already, good things are coming out of it."

The critics also underestimate Gerry Rubin, says Ruderman. She joined the HHMI Medical Advisory Board just as Rubin and HHMI's new president Tom Cech were unveiling the first outlines of what would become Janelia. Ruderman remembers, "When this was presented to the advisory board, there was a lot of very candid discussion. A lot of it was positive, but there were some very hard

questions asked. Besides being good at [creating] big visions, Gerry has excellent scientific taste, high energy, and a totally positive attitude that allows him to really listen to criticism and to take advice. The idea benefited from a continuing discussion of what Janelia should be, as well as the practical side of it."

From First Principles … and Boston

Another key advisor during the planning process and a current member of Janelia's Advisory Committee was Maxine Singer, now the Emeritus President of the Carnegie Institution of Washington. "Fashioning a place from first principles has advantages and disadvantages compared to coming into a place that's functioning. It's an experiment, but like all good experiments, it's based on previous work," says Singer.

"Gerry gets total credit for the planning of Janelia," Singer declares. "The laboratory building is amazing and unlike anything I've ever seen. It's a tremendous accomplishment, and we're all hoping that his vision really works out although it's much too early to tell. But it's finally there and it seems to be functioning very well. He's got terrific people helping him to run it. The whole design is attentive to what people might want and need."

If the roots of Janelia Farm are in Rubin's imagination, his roots are in Boston, as his still-strong native accent makes immediately clear. His parents weren't intellectuals, Rubin explains, but they strongly supported his education and that of his older brother, David (who is now a psychology professor at Duke University). His mother was a teacher. His father was a nonprofessional traffic engineer for the Massachusetts Highway Department who worked his way up from fixing traffic lights to designing intersections.

Rubin says that he must have tried his parents' educational ambitions sorely in elementary school, where he says he was a classic dreamy underachiever. Somehow, he awoke intellectually in time to ace the admissions test for Boston Latin High School. At the time he entered Boston Latin, Rubin recalls that biology was not taught because it wasn't considered a rigorous science. By the time Rubin entered MIT as an undergraduate in 1967, biology had become a rigorous enough science for the wizards of Kendall Square to start a Biology Department. The newly recruited faculty included David Baltimore, Harvey Lodish, and David Botstein.

Hooked On the Lab

It was Botstein who sent Rubin off to the summer undergraduate research program at CSHL and to Ray Gesteland's lab, where Rubin worked for two summers. "At that point I was hooked on the lab," says Rubin. He was also taken by Cold Spring Harbor's isolated campus, where the director lived on the grounds to receive questions and complaints at all hours. That would be a Janelia feature.

"When I went back to MIT for my senior year, I talked to Harvey Lodish about doing my doctorate at the MRC," Rubin recalls. And he said, 'Oh, just write a letter to Sydney Brenner,' which I did, and that was it. I was accepted. I think I had to show my transcript to the Cambridge registrar once I got there." At Janelia, group leaders would be seen in public and at the bench.

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A Record for Brevity

Finishing his Ph.D. in 1974, Rubin was in search of a postdoc position in a lab with strong biochemistry. (He remains intensely proud that his thesis still holds the MRC Cambridge record for brevity—42 pages including notes.) He'd heard Stanford's David Hogness speak at the MRC and took Brenner's advice that Stanford was the place for biochemistry. Thus Rubin arrived in the Hogness lab in September 1974, on the ground floor of the recombinant DNA revolution.

"One thing I've realized as I've gone along is how lucky I was early on," Rubin declares. Stanford had pioneered recombinant DNA technology and, at the time, it was one of the few places where it could be carried out. It was also Rubin's introduction to *Drosophila*, a once-popular model organism that had been out of favor while phages and simple animal viruses took center stage. Recombinant DNA would move *Drosophila* back into the spotlight. Hogness quickly set his newest postdoc to building *Drosophila* clone libraries.

"Again this was part of that string of good fortune. My whole career would have been different without cloning. It's a scientist's dream

to have a new set of tools that allows you to approach a problem in a way that makes you the first one there. It's like being the first one to land on an unexplored continent." Having the latest and the next technology would also become part of Janelia.

His experience with recombinant technology also made Rubin a hot item on the junior faculty market in the mid-1970s. "People were calling up David Hogness and asking if he had any postdocs looking for jobs," Rubin remembers. One of the places calling was HMS. He accepted a junior faculty position with a lab in the Dana-Farber Cancer Institute. Soon after came the approval of his first NIH grant. In those days it wasn't until the first renewal that anyone expected real results or asked hard questions, Rubin recalls.

Scientifically and personally, Rubin struck gold at HMS. The new DNA tools allowed him to explore *Drosophila* genetics in unprecedented detail and precision. He also found the love of his life, managing a lab down the hall at Dana-Farber. His wife-to-be Lynn Mastalir told him later that falling in love with someone at work was his only hope because he worked all the time. At Janelia, Rubin would insist on a family-friendly environment.

Lynn and Gerry's son, Alan, was born in 1980, just before they left Boston for Baltimore and the Embryology Department of the Carnegie Institution of Washington. When Rubin went to his Dana-Farber chairman to announce that he was leaving, his chairman asked if there was anything Harvard could do to change his mind. Rubin remembers the interview with a grin. "I told him that I was going to a place that didn't give tenure. I would be getting only two-thirds of the lab space I now had and that I was taking a 15% cut in salary. I said, 'I know you could match all these terms, but it wouldn't change my mind.'"

P Elements Advance

The lure of the Carnegie for Rubin was its small-scale, low-key collegiality, and its emphasis on collaboration. At the Carnegie, Rubin found his best all-time scientific collaborator, Allan Spradling. What they discovered together in 1982 was a major breakthrough, according to Spyros Artavanis-Tsakonas of HMS. Rubin and Spradling used "P elements" in the *Drosophila* genome to genetically engineer for the first time the germ-line of a multicellular animal. "It was major," says Artavanis-Tsakonas. "At the time, we had all kinds of genetic techniques and all kinds of cytological advantages but we could not really transform flies. This immediately opened up structure–function relationships in a way that revolutionized the field. It was nothing short of that, frankly."

"When I arrived in his lab, Gerry was focused on sequencing the [*Drosophila*] genome," remembers Andrea Page-McCaw. "But he would swoop in from time to time and offer the best advice—the advice that allowed my project to move forward so that I can be an independent scientist today."

Artavanis-Tsakonas, who has known Rubin since their MRC grad school days, also knew firsthand the difficulty of Rubin's breakthrough. "He beat me to it," Artavanis-Tsakonas says with a laugh. "I wasn't angry at all. Gerry did it the right way. I was doing it the wrong way. That's the way it goes. Once he and Allan had characterized the P element, it was an obvious link to try. With his characteristic intellectual courage and his lethal efficiency, he solved the problem with Allan, who is no slouch either."

The P element transfer technique raised new research possibilities and then there was the prospect of someday sequencing the entire genome of a multicellular animal. To scale up for projects of such size, Rubin felt he would need a bigger lab and greater resources. In 1983, he stepped out of small science at the Carnegie and into big science at the University of California, Berkeley, as the John D. MacArthur Professor of Genetics. In 1987, he was made an HHMI Investigator at Berkeley and elected to the National Academy of Science. He was 37.

No Way to Run

From his time at the Carnegie, Rubin took for Janelia a passion for collaboration and from Don Brown, his Carnegie chair, his central administrative philosophy: "Democracy is no way to run a research institution." Declares Rubin, "I've told everyone who comes to Janelia, that as long as I'm director, they'll never be asked to vote on anything, but their opinions will always be asked and considered."

Correction: The Profile of Dyche Mullins in the May 2007 issue of the *ASCB Newsletter* misspelled the name of Roger D. Sloboda, who was one of the legendary instructors at the 1973 MBL Physiology Course in Woods Hole.

At Berkeley, Rubin became known as a master of mass organization. He headed up the Berkeley *Drosophila* Genome Project, but, in 1998, he stunned the academic sequencing community. He accepted Craig Venter's offer to use the controversial shotgun sequencing technique on *Drosophila* that had been developed at Venter's commercial biotech firm, Celera Genomics. Venter hoped to demonstrate that the Celera approach could sequence the human genome faster and just as accurately as the academic consortium that opposed him. Rubin just wanted a faster and cheaper way to fully sequence *Drosophila*. In 2000, Rubin gathered together a consortium of 60 *Drosophila* geneticists, computational biologists, and number crunchers for a marathon "annotation jamboree" that sorted out Celera's "release 1 version" of the genome into 13,600 genes.

From managing the genomic alliance, Rubin brought to Janelia Farm the confidence to handle complex projects, multidisciplinary skill sets, and potentially difficult personalities. "Ambitious people are motivated by what we think will have the biggest impact," Rubin explains. "I decided many years ago that, for the remainder of my career, I could have a much bigger impact on science facilitating the work of others by managing big projects."

What Can't Be Fixed

Janelia is the biggest thing Rubin could imagine. "Young people today don't have the opportunities that I had. I can't fix that, but I can help build an environment here for some number of scientists who are motivated by the love of discovery and can work in collaboration." It's his way of giving back some of his good luck. "It's like I told all my postdocs: My job is to make sure that you have the freedom to choose a problem that interests you and the resources to do the experiments. If you aren't successful, it will be because you are not smart enough or you didn't work hard enough."

Last August, Rubin shut down his lab in Berkeley and opened his new one at Janelia. He also moved with Lynn into the only single-family home on the Janelia campus, the Director's House. Their son, Alan, now lives in Seattle, where he is a grad student in computational biology at the University of Washington. Leaving Berkeley finally forced Rubin to drop his 23-year season tickets to Golden Bear football and basketball games.

Andrea Page-McCaw, who is now at Rensselaer Polytechnic Institute, was one of Rubin's last postdocs in Berkeley. Rubin expected his postdocs to be nearly independent investigators who relied on him chiefly for space, funds, and timely scientific advice. "That's what I was looking for and that's what I got," says Page-McCaw. But he would swoop in from time to time and offer the best advice—the advice that allowed my project to move forward so that I can be an independent scientist today."

Rubin's old friend from grad school days, Artavanis-Tsakonas, agrees that much of Rubin's success has come from his ability to size up talent and put it to good use. As a mentor, Rubin has few peers, says Artavanis-Tsakonas. "The biggest measure of Gerry's success has been his scientific progeny, his postdocs, and grad students. A stellar group of people has come out of his lab," according to Artavanis-Tsakonas. ■

—John Fleischman

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The ASCB 2007 Call for Award Nominations

Norton B. Gilula Memorial Award

Who is Eligible: An outstanding graduate or undergraduate student who has excelled in research

How to Apply: The student or advisor should submit a one-page research statement, a list of publications, if any, the abstract submitted to the current year's Annual Meeting, and the advisor's letter of recommendation. Duplicate applications from graduate students may be submitted for the Gilula and Bernfield Memorial Awards.

Awards: The winner is presented a plaque. Expenses to attend the Annual Meeting are paid.

Deadline: August 1

Merton Bernfield Memorial Award

Who is Eligible: An outstanding graduate student or postdoctoral fellow who has excelled in research

How to Apply: The student or postdoc or his or her advisor should submit a one-page research statement, a list of publications, a copy of the abstract submitted to the current year's Annual Meeting, and the advisor's letter of recommendation. Postdocs may also submit the recommendation of their graduate student advisor. Duplicate applications from graduate students may be submitted for the Gilula and Bernfield Memorial Awards.

Awards: The winner is presented a plaque and will speak in a Minisymposium at the Annual Meeting and receives financial support to attend the Annual Meeting.

Deadline: August 1

All applications and nominations should be submitted to:

The American Society for Cell Biology
8120 Woodmont Avenue, Suite 750
Bethesda, MD 20814-2762
ascbinfo@ascb.org

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