Elliot M. Meyerowitz

The new post came with a key to the garden gate. When Elliot Meyerowitz agreed to a two-year term as Inaugural Director of the privately financed Sainsbury Laboratory at the University of Cambridge, he was given a brand new building, a mandate—and the means— to fill it with plant molecular biologists, and a key to the Cambridge University Botanic Garden that surrounds it. The key to the gate has turned out to be a wonderful perk, says Meyerowitz, who now commutes on foot from the townhouse where he and his wife, Joan Kobori, are living straight across the garden to his new lab.

The Botanic Garden owes its foundation to John Stevens Henslow, better known today as the man who recommended Charles Darwin for the post of gentleman-scientist on HMS *Beagle.* Young Darwin was supposedly studying for the ministry at the time but was better known around Cambridge as "the man who walks with Henslow," botanizing and theorizing. "I walk through the garden where Henslow and Darwin used to walk up and down, thinking about variation in organisms," Meyerowitz reports, "I get to walk on that path every morning."

Meyerowitz has a knack for pathways. Along with a small number of key scientific allies, Meyerowitz is best known as the inventor of *Arabidopsis*, not the plant itself, *Arabidopsis thaliana*, a.k.a. the mouse-ear cress, but *Arabidopsis*, the molecular and genetic model organism that has swept plant biology into the 21st century.

Trained as a "drosophilist" in grad school at Yale and as a postdoc at Stanford, Meyerowitz set up his own fly laboratory in 1980 at the California Institute of Technology (Caltech) in Pasadena. Within a year, he'd branched out into *Arabidopsis*, an obscure Alpine flower that was one of many such experimental plants going back to Gregor Mendel that were used sporadically in genetics research. His interest in plants dated back to Yale when Meyerowitz would sit in on plant developmental biology seminars and leave wondering if the new molecular technologies transforming fly biology could be transferred to the plant kingdom. By 1993, the Meyerowitz lab was all *Arabidopsis* all the time.

In 2009, the National Science Foundation (NSF) reported that nearly 3,000 peer-reviewed *Arabidopsis* papers had been published the year before, a 10-fold increase in six years. *Arabidopsis* publications now overshadowed those of all other plants, including the mighty *Zea mays*. Today *Arabidopsis* might even rival the classic lab models of fly and worm as the arena for cutting-edge experiments on the fundamental mechanisms of development, genetics, translation, and signaling.

Thomas Hunt Morgan Sat Here

Meyerowitz had a hand—a small hand, he insists—in much of this. Technically on leave from Caltech where he remains the George W. Beadle Professor of Biology and a Howard Hughes Medical Institute–George and Betty Moore Foundation investigator, Meyerowitz wears his honors and his own importance very lightly. He was Chair of the Biology Division at Caltech for a decade, a job originally held by the founding father of fly genetics, Thomas Hunt Morgan. A lot of people have had the job since, says Meyerowitz, brushing it off. Meyerowitz is, among other things, past president of the Genetics Society of America and of the Society for Developmental Biology, a member of the National Academy of Science, a Foreign Member of the Royal Society, and an awardee of the Japan Society for the Promotion of Science. He's been an ASCB member since 1997, served 10 years as an Associate Editor of the Society's journal *Molecular Biology of the Cell*, and was a candidate for President of the ASCB. He has two grown sons, a wife who is adapting to Cambridge life, and a growing passion for a new kind of predictive experimentation that uses mathematical modeling to lay out beforehand exactly what a given hypothesis should look like. That way your lab or another one halfway around the world can compare bench results to computational predictions. He calls the process making the hypothesis explicit.

The explicit reasons for the rise of *Arabidopsis* are easy to enumerate, says Christopher Somerville, who along with Meyerowitz is widely credited with masterminding the *Arabidopsis* revolution. Somerville is now Director of the Energy Biosciences Institute at the University of California, Berkeley.

Credit: Eric Reed/Ap and Howard Hughes Medical Institute

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Somerville and Meyerowitz won the 2006 Balzan Prize for "plant molecular genetics," splitting half of the one million Swiss franc (CHF) prize, with the other half million CHF going to young investigators who the winners were able to nominate. According to Somerville, *Arabidopsis* was the ideal candidate to become the plant version of *Caenorhabditis elegans* because it had a small genome, a quick life cycle, and a small footprint. You can grow *Arabidopsis* indoors in a Petri dish without exotic irrigation or lighting systems. "Genetics requires a big population," says Somerville, "and I could probably grow 5,000 of them right here on my desk." *Arabidopsis* is also incredibly fecund—a single plant can produce 20,000–30,000 seeds in its six-week life. Another *Arabidopsis* virtue, at least to Somerville and Meyerowitz, was its non-useful status. No one was growing *Arabidopsis* for agriculture or horticulture. In some quarters, that remains a major objection to *Arabidopsis* research, according to Somerville. "It's still called the 'A-word' at the USDA."

Arabidopsis is not on the U.S. Department of Agriculture's list of 140 "plants of utility" for research funding, but that, in Somerville's eyes, is another plus. Before *Arabidopsis*, basic plant research was spread out over too many species, says Somerville. "Just imagine people working in 140 species of *Drosophila* or 140 species of nematodes. But there was tremendous resistance in the beginning."

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Meyerowitz was critical in countering that resistance and developing support for the tool-making necessary for a modern lab organism, says Somerville. "Right from the beginning, we went to the NSF and said that there was this possibility of getting a model organism with good properties and applying molecular biology to it." Along with some support from the Department of Energy, the NSF underwrote the scientific infrastructure for *Arabidopsis*—yeast and bacterial artificial chromosome libraries, seed stock centers, a genetic and molecular database, newsletters, annual reports, and *Arabidopsis* meetings. Somerville was a prime mover behind The *Arabidopsis* Information Resource online database, which today gets 36 million hits a year, but he insists that it was Meyerowitz's patient behind-the-scenes work on the "social infrastructure" that was crucial. In the burgeoning *Arabidopsis* community, Meyerowitz made sure that information, mutants, and hot ideas were widely and immediately shared. Somerville also credits Meyerowitz's low-key but tireless leadership of the Multinational *Arabidopsis* Steering Committee (MASC) for making *Arabidopsis* a global enterprise. MASC rounded up labs and government support in the United States, Europe, and Japan for the sequencing of the *Arabidopsis* genome. The news about the *Arabidopsis* genome was almost lost in the hoopla surrounding the almost simultaneous publication of the human genome in December 2000, but *Arabidopsis* was the first plant genome ever sequenced. "And we did a better job," says Somerville.

The *Arabidopsis* model was bearing fruit in the Meyerowitz lab long before. In the early years, Meyerowitz produced the first precise confirmation that the *Arabidopsis* genome was small—136 megabase pairs. His lab cloned the first *Arabidopsis* gene, populated restriction fragment length polymorphism marker maps, and cloned the first hormone receptor in plants.

The Buzz about Plants

It was an exciting place to work, says Caren Chang, now at the University of Maryland, College Park, who joined the Meyerowitz lab in 1985 as a grad student and stayed on for two postdoc tours. Her original choice was more or less a hunch, Chang recalls. "It wasn't that I liked plants, but there was all this talk that Elliot was doing something really different." The buzz got louder over time, attracting a bumper crop of students and postdocs who have gone on to exciting *Arabidopsis* careers of their own, including Chang, Martin Yanofsky, John Bowman, Steve Jacobsen, Detlef Weigel, Xuemei Chen, and Jian Hua.

At first though, Chang found Meyerowitz's sheer intelligence intimidating and his lab bewildering. She soon adapted. There was his office for one thing. It doubled as the staff lounge. Everyone was welcome in Elliot's office, day or night, whether he was there or not, Chang remembers. You could walk in to make coffee, chat while a gel ran, or ask a detailed technical question. Besides a stack of journals, Meyerowitz subscribed to a garish supermarket tabloid with stories about the undead Elvis and extraterrestrials. "It was right there with *Science* and *Nature*," Chang says. Meyerowitz kept the lab computer—there was only the one in the early days, a first edition Macintosh—next to his own Mac, so lab members who were working on papers sat virtually at his elbow. Nothing phased him. "Crystal Quest," an early video game, was installed on the Mac and a playpen was set up near his desk. "Someone in the lab had a baby so there was a baby in there with him for a while," Chang recalls. "We just hung out in his office and it made for great discussions." Later when

Meyerowitz moved to larger quarters, he insisted that his new office open directly onto the new staff lounge. His door remained open.

Chang arrived early enough to see the Meyerowitz fly group wither away while his *Arabidopsis* team spread through a warren of small, ill-equipped rooms on different hallways and floors at Caltech. "It was the worst space, definitely not state-of-the-art." The dissecting scope was in a particularly dingy basement room. Chang recalls the day, "Elliot went down there and a few hours later he suddenly runs upstairs and announces to everyone that he had homeotic mutants. And that was what led to the ABC model."

The Meyerowitz lab used the *Arabidopsis* floral mutants to identify three classes of genes, grouped for simplicity as A, B, and C, that act in concert as master regulators of the four concentric rings or whorls of the flower—the sepal, petal, stamen, and carpel. Expressed alone, silenced, or in combination from adjacent rings, the three gene classes encode precise transcription instructions for each whorl. Activated class A genes in the outermost whorl create sepals. Expressed together, class A and class B create petals in whorl two. Class B and class C genes expressed in the same domain give rise to stamens in whorl three. Class C genes create the central carpels in whorl four. The discovery in plants of genes with functions similar to those of the gene sets that define segmentation and polarity in *Drosophila* embryos electrified the field.

Interestingly, the best confirmation of the ABC model came from an older plant model, the common snapdragon, *Antirrhinum majus*, grown in the UK laboratory of Enrico Coen at the John Innes Centre in Norwich. As experimental subjects, snapdragons go back to Darwin's own greenhouses. *Antirrhinum* was in vogue early in the 20th century during the rediscovery of Mendel's work, but the snapdragon was shouldered aside by the rise of corn genetics. A collection of *Antirrhinum* flower mutants survived at the Innes, and Coen used them to identify snapdragon genes that seemed to operate in combination to define flower development. Coen knew about *Arabidopsis* and Meyerowitz, but the first clue that they were on converging paths came from a Meyerowitz postdoc, Marty Yanofsky (now at the University of California, San Diego). Yanofsky heard Coen speak about his *Antirrhinum* results and came up afterward to say that the Caltech lab was working along similar lines in *Arabidopsis*.

Snapdragons Speak

Isn't that every scientist's worst nightmare? Coen laughs. "Was it a shock? Well, it was great news in a way. It gave us more confidence that this theory had general validity." It also helped that Meyerowitz was eager to learn the *Antirrhinum* side of the picture, inviting Coen to Caltech and asking him to collaborate on a review article already commissioned by *Science.* The resulting 1991 paper with the engaging title of "War of the Whorls" was a true collaboration, says Coen. Among other things, Meyerowitz accepted Coen's ABC terminology for the gene classes to widen the relevance of the model. "One of the worries when you come up with a theory is that it's very specific to your system, but this opened everything up," Coen explains. "People had been looking at these weird mutants for years but there seemed to no rhyme or reason. There is a fair taxonomic distance between *Arabidopsis* and *Antirrhinum*, so it was reassuring to find that what we were both saying was pretty much the same."

Looking back, Meyerowitz says that one effect of the ABC model was to push him to explore computational biology. "It became clear early on that there were a number of feedbacks, but there were also feed forwards," Meyerowitz explains. "What happened later fed back to what happened earlier. If some developmental event didn't happen, some stem cell population would be signaled back to. It wasn't entirely hierarchical and yet you had to have some way of modeling it." More recently, Meyerowitz has made exploring "the interface between developmental genetics and computational modeling" the central focus of the new Sainsbury Laboratory in Cambridge.

Having Meyerowitz in Cambridge just up the road from Norwich, at least temporarily, has been a real boon for Coen. He's had Meyerowitz down to the Innes Centre and toured the new lab as Meyerowitz labored to turn on the heat, hire staff, and recruit group leaders. "It's a beautiful building in the heart of the Botanic Garden and, of course, Elliot has the key to the gate," says Coen. "One night I remember walking from the lab back to his house for dinner through the garden. It was pitch black and you could hear birds and things moving about. It was such a strange sensation in the middle of Cambridge. Elliot was loving it because he does it every day. He was in his element." ■

—*John Fleischman*

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