

Biography of John F. Doebley

Several thousand years ago, farmers living in Mexico transformed a wild grass called teosinte into modern maize through rounds of selective breeding for large ears of corn (1). Although this much is certain, a multitude of questions surround the mechanisms underlying this feat of pre-historic genetic engineering. How many genes contributed to the evolution of each new trait? What types of genes were involved? And do the alterations in these genes affect protein function or gene expression?

To answer these and related questions, John F. Doebley, genetics professor at the University of Wisconsin, Madison, has spent the past two decades examining the genetic differences and similarities between teosinte and maize (*Zea mays*). Doebley and his laboratory members pioneered the use of quantitative trait locus (QTL) mapping (2–4) to successfully identify which regions of maize’s genome are responsible for several “domestication traits,” features that separate maize from its undomesticated relatives. His team was one of the first to clone genes identified through QTL mapping, including a pivotal domestication gene known as *teosinte branched1* (*tb1*), which affects kernel structure and plant architecture (5).

Doebley’s work has earned him several awards, including election to the National Academy of Sciences in 2002. In his Inaugural Article (6), published in this issue of PNAS, Doebley and colleagues determined that selecting for *tb1* thousands of years ago did not affect genetic diversity at neighboring genes. This conclusion clarifies how the maize genome was sculptured by past selective breeding and can help elucidate how the genomes of other organisms respond to selective pressure.

A Foot in Two Fields

Inspired by a love for nature, Doebley began his undergraduate education as a biology major at West Chester State College in West Chester, Pennsylvania. However, after taking a class taught by a particularly engaging anthropology professor, Marshall Becker, Doebley switched his major to anthropology. Doebley recalled that Becker went out of his way to involve students in research. “He took us to the national meeting for the American Anthropological Association, and he brought speakers from around the country to our little school. They’d give us lectures, and afterwards they’d meet with us for din-



John F. Doebley, photograph taken in 2003.

ner,” said Doebley. Becker also operated a small archeological site just outside West Chester and encouraged his students to accompany him on excavations. “He did a tremendous job of getting the undergraduates involved in anthropological research and also in scientific thinking: the idea that we could query nature and get an answer,” Doebley said.

After he graduated with a degree in anthropology in 1974, Doebley immediately entered a master’s program in anthropology at Eastern New Mexico University in Portales. Rather than abandon his interest in biology, he nurtured it in graduate school by incorporating classes like genetics, ecology, and primatology into his degree program. “Despite being an anthropology student on paper, I found that biology, and genetics in particular, held a special interest for me,” he said.

On completing his master’s degree in 1976, Doebley took a year off to work as an archeologist with the University of Missouri and then entered the Ph.D. program in anthropology at the University of Wisconsin. “My intention at this point was to study genetic variation, blood groups and such, in humans, with the idea that I could help trace the diversification of human populations,” he remembered. He soon realized that this would be an uphill battle, and he began thinking about switching fields again. “Strangely, while an anthropology student at Wisconsin, I never actually enrolled in any anthropology courses. I enrolled in courses in biochemistry, zoology, and botany,” he said. “I must

have known that I would be going back to biology.”

Through a lucky set of circumstances, Doebley became acquainted with botany professor Hugh Iltis, an experience that would forever change the course of Doebley’s career. Complaining to one of the other anthropology graduate students, Iltis remarked that anthropologists knew too little biology and nothing about plants. In defense, the student mentioned Doebley as an anthropologist who knew plenty about biology. “So Iltis said, ‘Send him over. I’ve got a job for him,’” Doebley recalled. Iltis invited Doebley to join his research project on the taxonomy of maize’s wild relative teosinte, a project Iltis had been involved with for many years. Doebley accepted and applied the next day to change his major from anthropology to botany. “I leapt for it, not knowing how it would work out,” Doebley said.

Doebley and Iltis traveled to Mexico to find sites where teosinte grew. After collecting specimens, the team made morphological and ecological observations and sorted the plants into groups based on these results. The Iltis team discovered a new teosinte species in the process, a perennial they named *Zea diploperennis*. Doebley published three papers on this research for his doctoral thesis (7–9) and completed his degree in 1980.

The following year, Doebley began a postdoctoral position at North Carolina State University, Raleigh, under the mentorship of geneticist Major Goodman. For several years prior, Goodman had studied allozymes, a type of genetic marker, to determine relationships between different varieties of maize. Doebley suggested to Goodman that they use allozymes to determine the evolutionary relationship between teosinte and maize. Within a few years, this research had netted the two scientists five papers (10–14). The most surprising result was that a particular form of teosinte, *Z. mays* subspecies *parviglumis*, was essentially genetically identical to maize. “By prior criteria, one would not have predicted that this teosinte should be so closely related to maize. You could almost say they look nothing alike,” said Doebley. Later, Doebley concluded that

This is a Biography of a recently elected member of the National Academy of Sciences to accompany the member’s Inaugural Article on page 700.

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parviglumis is the specific subspecies that was selectively bred by ancient farmers and eventually became modern cultivated corn (15).

In 1982, recognizing that molecular biology, and not allozymes, was where evolution and the study of genetic variation were headed, Doebley took a second postdoctoral position at North Carolina State University with mentor Ronald Sederoff. “Ron was a real guiding light for me. Although we never published together, I learned a great deal from him,” Doebley said. In Sederoff’s laboratory, Doebley learned a variety of molecular genetics techniques, including isolating and cloning DNA, purifying chloroplasts and mitochondria, and making gene libraries.

A Career Takes Root

In 1984, Doebley began his first professorship at Texas A&M University, College Station. For the next 3 years, he taught and developed a research program in the evolutionary genetics of maize. An attractive job offer, a cooler climate, and a yearning to find greener pastures for maize research swayed him to take a job at the University of Minnesota, St. Paul, in 1987. It was during his tenure at Minnesota that Doebley’s work earned him wide recognition in the emerging field of complex trait genetics.

Working from an idea that he had developed during his postdoctoral years at North Carolina State, Doebley used QTL mapping to search for regions of the genome that gave domesticated corn different traits than its ancestor teosinte. He and his colleagues discovered that most trait differences between the two species, such as few versus many ears, were under multigenetic control. However, for several of the traits, the researchers could identify one region of the genome that controlled most of the difference. For example, a region on chromosome 4 largely controlled the formation of a casing that surrounds teosinte kernels but not those of maize. The team published their results in PNAS in 1990 (2).

Doebley immediately turned his laboratory’s focus toward pinpointing and cloning one of the principle genes involved in the evolution of maize, known as *teosinte branched1*, or *tb1* for short. On reaching this goal in 1997 and subsequently publishing their findings in *Nature* (5), Doebley’s group tackled a more complex task: identifying how *tb1* operated to produce more branches in teos-



Doebley’s current laboratory group, left to right: Landen Rentmeester, Tina Nussbaum Wagler, Richard Clark, Yves Vigouroux, Joan Zhao, Laura Vaughn, Kirsten Bomblies, Anne-Celine Thuillet, and Peter Rose.

inte and fewer branches in maize. Through examining *tb1*’s molecular evolution, the researchers inferred that the crucial differences were in the gene’s regulatory region rather than its protein coding region. Essentially, the two species produce the same protein that controls branching, but maize produces significantly more, effectively reducing the plant’s number of branches. Because plants with fewer branches grow larger ears of corn, Doebley’s team suggested that prehistoric farmers selected for a lower branch number, thus fixing *tb1* in its present state in cultivated maize. The researchers published their findings in *Nature* in 1999 (16).

Again on the move, Doebley returned to his alma mater, the University of Wisconsin, in 1999. He soon recruited postdoctoral associate Richard Clark, who took the lead on the study of *tb1* (6). Along with colleagues Eric Linton and Joachim Messing, Clark and Doebley extended earlier work by asking whether *tb1*’s neighboring genes became fixed when *tb1* was selected for, an effect known among evolutionists as “hitchhiking.” After comparing the sequences of many maize and teosinte stocks, the researchers found that genetic diversity at a neighboring gene was remarkably high, suggesting that *tb1*’s neighboring genes were unaffected by selection on *tb1*. The team’s findings have implications for plant breeding: “It says that you can apply selection for fa-

vorable genes without severely reducing variation even at tightly linked genes. That’s a plus, because breeding everything to fixation would reduce the future ability of breeders to make maize even better,” Doebley said.

No Commercial Grain

Currently, Doebley and his laboratory have a variety of ongoing projects aimed at improving the understanding of links between genotype and phenotype in maize and teosinte. The group continues to use QTL mapping and other techniques, such as reverse genetics, to locate genes that code for specific domestication traits in maize. Doebley has even started a “redomestication” project to determine how long it might have taken to domesticate maize from teosinte. “I think in as few as 25 years I can move teosinte fairly far along the road to becoming maize,” he predicts. After planting a site in Hawaii with teosinte subspecies *parviglumis* seeds in September 2002, he expects to reap the first round of results this February (www.wisc.edu/teosinte). Such experiments often catch the attention of seed companies eager to cash in on making corn a better crop through genetic modification. However, Doebley says his interests run more toward the academic than the commercial. “I never think in terms of applications or improvements of corn,” he said. “I’m doing this because it’s fun.”

Christen Brownlee, *Science Writer*

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