PNAS PROFILE

Profile of Joy M. Bergelson

Beth Azar, Science Writer

Evolutionary biologist Joy Bergelson is fascinated by the question of how organisms survive attack by their antagonists. Her organism of choice, *Arabidopsis thaliana*, a flowering annual plant, faces a raft of threats from viruses, bacteria, fungi, mollusks, and insects. Bergelson, a professor of genomics at New York University, uses genetic engineering and molecular biology to examine how plants evolve to resist disease. She has helped dispel a long-held belief that plants and microbial pathogens evolve through an arms race, pioneered transgenic techniques for studying plant evolutionary ecology, and performed studies of plant microbiomes. Elected to the National Academy of Sciences in 2018, Bergelson examines the heritability of plant microbiomes in her Inaugural Article (1).

Joy M. Bergelson. Image credit: Michelle Litvin.

Scientific Method

Born in Brooklyn, NY, Bergelson grew up in Metuchen, NJ. Her father was a communications engineer, and her mother stayed home with Bergelson and her brothers before taking up an administrative job at Rutgers University. During high school, Bergelson earned early work experience, advocating for a bottle recycling bill in New Jersey through the school's ecology club. The experience motivated her to pursue environmental law. In 1980, she set off for Brown University, a waystation on her journey to law school. However, during her sophomore year, when Bergelson took comparative literature alongside invertebrate biology, her outlook changed. "The science people were telling me to be creative, and disciplines where I thought I should be creative were telling me to use the scientific method," she says. "I figured I might as well learn how to use the scientific method correctly, so I tried other science classes and eventually got completely hooked."

As a biology major, Bergelson studied dragonfly foraging behavior with evolutionary biologist Jonathan Waage and published her first scientific article (2). She also developed an interest in plants from evolutionary biologist Johanna Schmitt. Most influential was her relationship with theoretical ecologist Peter Kareiva. "He's extremely critically minded," says Bergelson. "He taught me to question everything and pull the essence of things out." Her mentors convinced Bergelson to apply for a Marshall Scholarship, which funds American students seeking a graduate degree in the United Kingdom. "I applied and went straight from college to the University of York to work with John Lawton to study plant–herbivore interactions," she recalls. "That's where I became interested in herbivory and enemies of plants."

After 2 years and an MPhil degree, Bergelson followed Kareiva to the University of Washington in Seattle, where he had relocated. Bergelson was interested in how plants' spatial structure—whether they grow uniformly or in patches—affects their interactions. For her doctoral work, she modeled competition between plants by manipulating their structure in a plot of land (3, 4). A slug attack changed the course of her career. The attack illuminated an influential layer of herbivores—slugs, insects, and microbes—on top of the plant patterning. In fact, Bergelson says, "the plant spatial patterning affected the rate of herbivory maybe more than the plant–plant competition.

Molecular Biology to the Rescue

Bergelson's thesis was in ecology, but her blossoming interest in herbivores, combined with her deep love of experimentation, sparked an interest in the mechanisms driving plants' interactions with herbivores and pathogens. Lunchtime seminars hosted by the university's botany department exposed her to the nascent field of genetic engineering. No one had cloned plant resistance genes yet, but once they did, she reasoned, she could start designing the studies she wanted. "I became determined to learn enough molecular biology to ultimately manipulate a plant's phenotype," Bergelson says. When she finished her PhD in 1990, she accepted a junior faculty

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This is a Profile of a member of the National Academy of Sciences to accompany the member's Inaugural Article, e2201285119, in vol. 119, issue 30.

Published August 22, 2022.

position at Oxford University, where she taught field ecology and learned the basics of molecular biology from the junior faculty. Meanwhile, ecologist Robert May acted as her intellectual mentor. By then, Bergelson was working on *Arabidopsis*, the model plant of choice for molecular biology.

In 1992, Bergelson took a job at Washington University in St. Louis. Three years later, researchers cloned the first plant resistance gene *Rpm1*; by this time, Bergelson had moved to the University of Chicago to be close to her future husband, molecular evolutionary biologist Martin Kreitman, with whom she was collaborating. *Rpm1* was a resistance gene for a disease caused by *Pseudomonas* bacteria. Although the topic did not concern herbivory, Bergelson says, "I went with it. And it was a good thing because it was years before any kind of herbivore resistance gene was cloned."

She started by testing the long-held belief, based on evidence from agriculture, that plants and their antagonists are in an arms race, fighting brief battles until both combatants mutate to higher levels of resistance and virulence. The idea implies that resistance genes should be evolutionarily young, constantly evolving to outsmart pathogens. Bergelson's team estimated *Rpm1*'s age by examining regions flanking the gene. Instead of finding a young gene, "we found just the opposite (5)," she says. "The allele was ancient. Resistance and susceptibility had been segregating for millions of generations. And that changed our question from "Can we demonstrate arms races?" to "How is selection maintaining this genetic stalemate?" she adds. The group described the phenomenon as a kind of ancient balanced polymorphism and found that it was relatively common. Indeed, since that first field study, Bergelson's laboratory examined many more resistance genes (6), finding that about one-third of the genes show evidence of ancient balanced polymorphism.

Rpm1 is an insertion/deletion polymorphism; the entire gene locus is missing in susceptible plants. Conveniently, this allowed Bergelson to create plants differing only in the presence or absence of the gene. Field research on thousands of transgenic plants demonstrated that resistance via *Rpm1* incurs costs to the plant in the absence of a pathogen (7); the costs counteract the known benefits of *Rpm1* resistance in the face of attack. In fact, in the absence of infection, plants with *Rpm1* produced 9% fewer seeds than plants without *Rpm1*. Bergelson and colleagues also found high costs of resistance for *Rps5*, another insertion/deletion polymorphism that harbors an ancient balanced polymorphism (8, 9). In contrast, *Rps2*, which has alternative alleles that appear capable of providing protection from pathogens, did not incur such costs (10). "So, what we find is that it's complicated," says Bergelson. "And the genetic architecture really matters when you're trying to understand the cost and benefit of particular genes."

Much of Bergelson's success has relied on developing new experimental techniques and pioneering strategies both in the laboratory and in large field experiments. A 20-year collaboration with evolutionary biologist Magnus Nordborg to develop *Arabidopsis* as a system for genome-wide association studies was foundational, proving that the plant has enough genetic variation to be useful, that its polymorphisms are structured enough to be mapped, and paving the way for the 1001 Genomes Project (11–13). She also developed methods and facilities for sophisticated field studies, including building the Warren Woods Field Station in Berrien County, Michigan, a field station in the United States that is among the first field stations to meet passive standards for energy efficiency.

Embracing Complexity

For years Bergelson felt stymied in her quest to understand how natural selection maintains ancient balanced polymorphisms. Little was known about natural *Arabidopsis* pathogens or the pathogen effectors to which resistance genes react. Researchers identifying resistance genes were largely working with agricultural pathogens from stock centers, not in nature. To understand natural evolution, Bergelson needed to study genes in an ecological context. "So, we started trying to understand the microbiome of *Arabidopsis* and identify some of the pathogens," she says.

Early work demonstrated that the bacterial pathogens *Pseudomonas syringae* and *Pseudomonas viridiflava* infect *Arabidopsis* in nature (14), and later work characterized the microbiome of *Arabidopsis* (15). A concerted effort to find pathogen effectors that *Arabidopsis* resistance genes recognize in natural populations led first to *AvrPphB2*, which *Rps5* recognizes. Because the cost of *Rps5* is large, Bergelson reasoned, the effector should be plentiful in nature for *Rps5* to be maintained in the genome. However, the effector is rare. Bergelson realized that the selection pressures on resistance genes must be more complex than theories suggested. She and her colleagues tackled this line of thinking in a 2014 article (9). They showed that while the pathogen carried *AvrPphB2*, it also carried another effector that interacted with *Rps5*, and that there are likely other pathogens carrying the same effectors that would also interact with Rps5. "It's a complicated ecological network, even when you consider the evolution of just a single gene," says Bergelson. "This work changed my whole perspective. Even to understand the interaction between two genes, you need it in its natural ecological context, and you need to embrace all that complexity."

Part of the natural complexity of plant–pathogen interactions involves a plant's microbiome, which, like the human microbiome, can benefit plant health and help fight disease. Another prong of Bergelson's research has been exploring the factors that influence the plant microbiome. The team found evidence that plants that share a genotype tend to share a microbiome (16). Bergelson's Inaugural Article (1) expands on that finding in a study that examined the leaf microbiomes of 200 *Arabidopsis* genotypes grown in northern and southern Sweden. They confirmed that the microbiome is heritable and then tested whether something about a host's genotype influences its microbiome. They discovered that only about 10% percent of the microbiome is heritable. "So, largely speaking, heritability is concentrated on just a fraction of the community, and that fraction is enriched for ecological hubs if you look at the network structure of the microbes," explains

Bergelson. "That opens the door to the possibility that one could reshape the microbiome through plant breeding because you could use the hubs as a kind of lever and shift the microbiome. That might be a more tractable problem than trying to change the environment to influence all the microbes."

Although Bergelson is not directly pursuing practical applications of her findings, she often thinks about ways to encourage others to make agriculture more sustainable and successful. Although she now lives in bustling Manhattan, she stresses the importance of a nature-focused perspective to agriculture.

1. B. Brachi *et al.*, Plant genetic effects on microbial hubs impact host fitness in repeated field trials. *Proc. Natl. Acad. Sci. U.S.A.* **119**, e2201285119 (2022).
2. J. Bergelson, Mechanistic interpretation of prey selection by *Anax junius* Larvae (Odonata: Aeschnidae). *Ecology* **66**, 1699–1705 (1985).
3. J. Bergelson, Life after death: Site pre-emption by the remains of *Poa anua*. *Ecology* **71**, 2157–2165 (1990).
4. J. Bergelson, Spatial patterning in plants: Opposing effects of herbivory and competition. *J. Ecol.* **78**, 937–948 (1990).
5. E. A. Stahl, G. Dwyer, R. Mauricio, M. Kreitman, J. Bergelson, Dynamics of disease resistance polymorphism at the *Rpm1* locus of *Arabidopsis*. *Nature* **400**, 667–671 (1999).
6. E. G. Bakker, C. Toomajian, M. Kreitman, J. Bergelson, A genome-wide survey of *R* gene polymorphisms in *Arabidopsis*. *Plant Cell* **18**, 1803–1818 (2006).
7. D. Tian, M. B. Traw, J. Q. Chen, M. Kreitman, J. Bergelson, Fitness costs of *R*-gene-mediated resistance in *Arabidopsis thaliana*. *Nature* **423**, 74–77 (2003).
8. D. Tian, H. Araki, E. Stahl, J. Bergelson, M. Kreitman, Signature of balancing selection in *Arabidopsis*. *Proc. Natl. Acad. Sci. U.S.A.* **99**, 11525–11530 (2002).
9. T. L. Karasov *et al.*, The long-term maintenance of a resistance polymorphism through diffuse interactions. *Nature* **512**, 436–440 (2014).
10. A. MacQueen, X. Sun, J. Bergelson, Genetic architecture and pleiotropy shape costs of *Rps2*-mediated resistance in *Arabidopsis thaliana*. *Nat. Plants* **2**, 16110 (2016).
11. M. Nordborg *et al.*, The pattern of polymorphism in *Arabidopsis thaliana*. *PLoS Biol.* **3**, e196 (2005).
12. S. Atwell *et al.*, Genome-wide association study of 107 phenotypes in *Arabidopsis thaliana* inbred lines. *Nature* **465**, 627–631 (2010).
13. 1001 Genomes consortium, 1135 genomes reveal the global pattern of polymorphism in *Arabidopsis thaliana*. *Cell* **166**, 481–491 (2016).
14. K. Jakob *et al.*, *Pseudomonas viridiflava* and *P. syringae*--Natural pathogens of *Arabidopsis thaliana*. *Mol. Plant Microbe Interact.* **15**, 1195–1203 (2002).
15. N. Bodenhausen, M. W. Horton, J. Bergelson, Bacterial communities associated with the leaves and the roots of Arabidopsis thaliana. *PLoS One* **8**, e56329 (2013).
16. M. W. Horton *et al.*, Genome-wide association study of Arabidopsis thaliana leaf microbial community. *Nat. Commun.* **5**, 5320 (2014).