PROFILE

Profile of Paul Schulze-Lefert

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Growing up on his family's farm in northwestern Germany, Paul Schulze-Lefert received an early introduction to plant biology that blossomed into a lifelong interest. In a fruitful career as a plant biologist, Schulze-Lefert has played a crucial role in elucidating mechanisms by which the plant immune system detects and fights harmful microbes, and his findings could lead to the development of pathogen-resistant crops. More recently, he has focused on fundamental questions about the complex interactions between plants and their microbial communities, called the plant microbiota. In his Inaugural Article (1), Schulze-Lefert describes the diversification of the bacterial microbiota in the roots of four plant species representing one phylogenetic lineage and shows that microbiota diversification is driven by host species–specific ecological adaptation and phylogenetic distance. In addition, he identified a few core bacterial families that were conserved over at least a 30-million-year evolutionary range and across biogeographical host specialization. For his many discoveries in the field of plant innate immunity and plant–microbe interactions, Schulze-Lefert was elected as a Foreign Associate to the National Academy of Sciences in 2010.

Schulze-Lefert, now the director of the Department of Plant–Microbe Interactions at the Max Planck Institute for Plant Breeding Research [Max-Planck-Institut für Züchtungsforschung (MPIPZ)] in Cologne, Germany, says he gained an early appreciation of the importance of plant domestication and breeding in human history. "Food production is of utmost importance in the face of a growing world population, and will be one of the grand challenges over the next decades," he says. "There is tremendous scope to improve not only yield, but also how we produce food."

To that end, Schulze-Lefert is focused on understanding how plants protect themselves from microbial pathogens. Current methods of crop protection use mainly chemicals to control harmful pathogens, but "I always felt that there was scope for alternative control of plant pathogens by using knowledge of the innate immune system," he says. "I think the time is ripe to apply this knowledge for breeding plants that are naturally resistant to pathogens."

Paul Schulze-Lefert. Image courtesy of Max Planck Institute for Plant Breeding Research.

Schulze-Lefert says his ultimate wish is for global crop resistance against pathogens. He cofounded a biotechnology startup called AgBiome that aims to use advances in plant biotechnology to improve crop resistance to pathogens and also advises the Two Blades Foundation, a charitable organization that supports research to develop disease-resistant crop plants. Schulze-Lefert has made major contributions to this goal through his research on understanding plant immune mechanisms, and his interest in this topic began as a graduate student.

Combining Plant Genetics and Biochemistry

Schulze-Lefert studied plant biochemistry and genetics at Marburg, Freiburg, and Cologne Universities. "It was the very early days of molecular genetics in the plant sciences," he says. Although his PhD was on light regulation in plants, Schulze-Lefert says his department was involved in investigating plant–microbe interactions. "Because of my PhD and my exposure to plant–microbe interaction research, I got hooked," he says.

Schulze-Lefert's doctoral studies emphasized the importance of a comprehensive approach that combined classical genetics with biochemistry. At the time, no systematic approaches had been undertaken to identify the molecules underlying genetically defined forms of plant immunity, and he saw an opportunity for a new research direction. Schulze-Lefert says he became interested in using the power of mutational analysis to tease apart the complex pathways involved in plant immune responses. "What still fascinates me about genetics is the ability to define first principles underlying complex processes such as plant immunity," Schulze-Lefert says.

However, Schulze-Lefert wasn't satisfied with understanding just the first principles; he wanted to uncover the details as well. "I think biochemistry and looking at enzymes and regulatory proteins helps you understand the beauty of molecular dynamics in a cellular context," he says.

The next step was to find a model plant that was amenable to both genetics and

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This is a Profile of a recently elected member of the National Academy of Sciences to accompany the member's Inaugural Article on page 585.

www.pnas.org/cgi/doi/10.1073/pnas.1321631111

molecular biology. The model plant that is currently used in plant research, *Arabidopsis*, had not yet been established, and there were many experimental systems in use. After receiving his PhD, Schulze-Lefert started working at the MPIPZ and says he started studying a crop plant: barley. "It was wonderful to do genetics with it, and I thought I could further develop the existing genetic tools and combine them with molecular biology to identify and pinpoint the molecular components needed for effective disease resistance responses," he says. His approach and choice of plant would soon pay off.

Isolating a Resistance Gene

In 1995, Schulze-Lefert moved to the Sainsbury laboratory in the United Kingdom for a senior research position, and it was there that he made a breakthrough. "It was then that I could do the expensive experiments, and really harvest the genetic material that we had prepared and isolate the underlying genes," he says. After years of effort, Schulze-Lefert was able to molecularly isolate a key barley resistance gene called *Mlo* (2). "This was for me a key event, and this is still one of my favorite results" he says.

Many researchers thought the barley genome was too complex for researchers to isolate resistance genes. "I felt that it wasn't more complex than the human genome, so there's no reason we should not be able to isolate the gene," Schulze-Lefert says. "It just needed perseverance, and careful preparation of genetic material, to achieve something that seemed impossible."

Although Schulze-Lefert first found *mlo*-associated resistance in a crop plant, it was then shown by his colleague Ralph Panstruga to also be effective in the model plant *Arabidopsis*. Schulze-Lefert still considers the isolation of *mlo* to be one of his breakthroughs, because its isolation from barley served as a springboard for demonstrating *mlo* resistance in other crop plants, including tomato and pea. In addition, this discovery enabled researchers to isolate several other genetic components of the innate immune system of plants.

A New Challenge

In 2000, Schulze-Lefert returned to Germany for a new challenge: to develop a department that was entirely dedicated to plant–microbe interaction research at the MPIPZ. He says he was inspired by his time in the Sainsbury laboratory and was also excited at the intellectual freedom afforded to him by the Max Planck Society. "It enables me to do the science that drives me, to really follow my instincts. I think that's something very precious, and I know that I'm privileged to study what my curiosity guides me to," he says.

Schulze-Lefert's curiosity led him to pursue multiple complementary research directions, one of which was what he calls "deep-drilling exercises," looking in detail at one class of immune receptors in plants called NOD-like receptors (NLRs). NLRs have been shown to act as intracellular sensors of pathogens, but precisely how they act is still unclear. For more than a decade, Schulze-Lefert has combined genetics and molecular biology to understand how NLRs function. "This is a wonderful intellectual exercise, but there is also the potential of applying our knowledge of these innate immune receptors to breed domesticated plants that are naturally resistant," he says.

Schulze-Lefert's work led to the identification of folding machinery for these NLR receptors, an advance in understanding how the receptors are assembled in the cell (3). He is currently investigating a family of NLR receptors that appear to have the capacity to initiate signaling both from the cytoplasm and the cell nucleus. Understanding this process would enable researchers to elucidate the interaction between NLR receptors and the plant transcriptional machinery. "This is another example where, year after year, one discovers new dimensions that are essential if one wants to understand key aspects of the innate immune system," Schulze-Lefert says.

In addition to studying how the plant immune machinery detects and responds to microbial pathogens, Schulze-Lefert also studies the pathogens themselves. He has been working with a fungal pathogen, powdery mildew, and has discovered features of its genome essential to its growth and pathogenesis (4, 5). This fungal pathogen had proved impossible to grow on synthetic media, a prerequisite for laboratory studies, and it wasn't until the pathogen's genome was sequenced as part of a collaborative and international team-building effort that the team discovered why. The researchers found that the fungus lacks a number of metabolic pathways, and, as a result, relies on nutrient uptake from living plant cells. "This lifestyle, the ability to grow only on living plant cells, has left its mark on the genome," he says. "That was a wonderful experience, to see how you can use genome-based technologies to understand the lifestyles of pathogens."

Although Schulze-Lefert continues his two-pronged approach, trying to understand both the plant immune system and the pathogens that attack it, a few years ago he decided to expand his research beyond diseases and pathogens and began to study plant interactions with microbial communities, known as the plant microbiota.

Understanding Plant Microbiota

The intellectual freedom Schulze-Lefert received at the Max Planck Institute played a decisive role in the expansion of his research activities about 4 years ago. Whereas his research had until then looked mainly at the interactions between one plant and one microbe, he now began to study how healthy plants interacted with entire communities of microbes in nature. "I think the time has come to apply reductionist approaches to these kinds of community interactions, and then to understand how these communities form and how they are beneficial to plants," he says. Early evidence suggests that the plant microbiota could play an important role in plant health and growth, similar to the functions of the gut microbiota of vertebrates.

Schulze-Lefert focused on the microbial communities living in plant roots, and how they influence nutrient uptake from the soil. "There is still very little knowledge of how plants solubilize nutrients from soil for growth, and I think soil microbes are key to better understand this process," he says. Schulze-Lefert sampled the soil bacteria that live in close association with *Arabidopsis* roots and was able to grow a substantial proportion of them in laboratory cultures. He then started studying the *Arabidopsis* root microbiota in carefully controlled synthetic bacterial communities, created by removing all of the microbes from *Arabidopsis* roots and then adding individual species of bacteria. This approach allowed the researchers to create a simple model for studying plant–microbe interactions, with minimal environmental fluctuations.

Teasing apart the *Arabidopsis*-associated microbiome allowed Schulze-Lefert's group to show that the bacteria that colonized *Arabidopsis* roots had a defined taxonomic structure, with preferential colonization by certain types of bacteria (6). In collaboration with plant biologist Jeffrey Dangl, the researchers found that similar microbial communities developed even when the plants were grown on different natural soils in Germany and in the United States.

According to Schulze-Lefert, there is now growing evidence that members of the root microbiota play crucial roles in helping plants solubilize and acquire nutrients from the soil for uptake by the roots. "Their function in nutrient uptake is analogous to our gut microbiota," he says. The root microbiota also appears to play a protective role. "I think there's accumulating evidence that these root microbiota organisms produce antimicrobial compounds that have protective functions against other soil-borne pathogens," Schulze-Lefert says.

Schulze-Lefert's work on plant microbiota represents "a tremendous intellectual challenge," he says. Unlike his previous work, where he could rely on an existing conceptual framework, "plant microbiota research is really in its infancy," he says. Going forward, he says he's excited at the idea of exploring this relatively new field. "This is now a completely new chapter of my scientific life, and it's a wide-open field. It's like being a schoolboy again, and just following your curiosity."

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