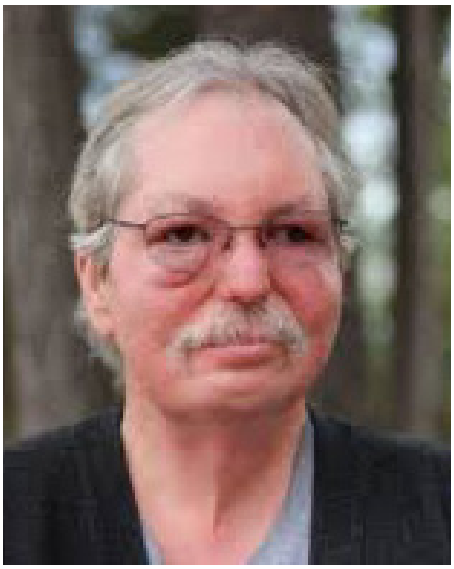
Jeffery Dangl



How did your career get started?

I grew up in a middle-class family in a small town in Northern California called Redding, where I spent most weekends fishing and hunting. My interest in science stemmed from an interest in wildlife and the wilderness. In second grade, I was very impressed when my father gutted a freshly caught salmon, and we found the heart was still beating. I was diagnosed with a rare form of muscular dystrophy at around age 10 and spent time in several hospitals as an experimental subject of sorts. At UCLA and at the Rancho Los Amigos Hospital in Downey, California, the pathologists encouraged me to look at my own muscle biopsy under the microscope. This fascinated me. My high school biology class was quite pathetic, but my chemistry course and teacher, Jon Lefler, was fantastic. He encouraged me to apply to Stanford, and I was overjoyed to be admitted.

I majored in both Biological Sciences and English (Modern Literature). I was lucky to, more-or-less, randomly land a summer job in Professor Len Herzenberg's lab, learning how to operate a Fluorescence-Activated Cell Sorter (FACS) that his lab had co-created to sort single cells at rates of thousands per minute based on various shape and fluorescent label parameters. I worked in Len's lab for two years and summers as an undergraduate, and for a gap year after graduation. Working in Len's lab was paradise for me. It was freewheeling but rigorous, and full of dedicated, creative scientists. I spent an academic term at Oxford University in England, studying the poetry of Yeats and Eliot and enjoying a very difficult and incredibly rewarding immunology tutorial under the guidance of Simon Hunt at the Sir William Dunn School of Pathology. Returning to Stanford, during my gap year I met my future wife and lab co-leader, Sarah Grant, then a doctoral student in Stanley Cohen's lab, and I was fortunate to be admitted to the Genetics Department's doctoral program in 1981.

The late 1970s and 1980s were a particularly exciting time at Stanford. Stanley Cohen and Paul Berg, along with Dale Kaiser and others, had essentially created the recombinant DNA revolution, and Len's lab, along with Irv Weissman and others, were rapidly expanding by utilization of the recent discovery of monoclonal antibody production to generate reagents of increasing sophistication for use with FACS to describe, isolate and study the many functional cell types of the mammalian immune system.

As an undergraduate and gap year student working with Len and post-doc Vernon Oi, I was given a project to generate a set of mouse monoclonal antibodies, each expressing one of the seven different mouse immunoglobulin heavy chains combined with identical antigen-binding sites for a fluorescent small molecule called DANSYL. We used both FACS enrichment and FACS clonal isolation of the rare isotype gene switching variants in our hybridoma line (around 1/10 million) and, for my doctoral project, recombinant DNA methods to produce this protein family. These proteins allowed us to assay functions encoded in the antibody's heavy chain, while keeping the antigen-binding site constant. We collaborated with Lubert Stryer to analyze the nanosecond-scale hinge region segmental flexibility of these molecules and demonstrated that the ability to fix complement correlated with higher segmental flexibility.

One day I was sent to the library to look up a new PNAS paper that Vernon thought was important. I found that paper, although I cannot remember what it was about. But I stumbled randomly onto another paper from Klaus Hahlbrock's lab in Freiburg, Germany, describing the cloning of some of the first plant defense genes. I was fascinated to learn that plants could respond to fungal cell wall extracts with transcriptional and metabolic re-programming. Given my immunology background and genetics training, I immediately wondered whether there was molecular specificity in this system and whether

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there were specific receptors that governed these responses. I extensively read genetics papers from Noel Keen, Al Ellingboe and H.H. Flor and realized that over the previous decades geneticists and plant breeders had generated a very rich background of material in the form of different cultivars expressing different disease resistance specificities. Moreover, it seemed evident to me that the plant defense response was ripe for molecular biology-based approaches.

I began attending the weekly plant biology seminars at the Carnegie Institute's Department of Plant Biology at Stanford and met Joe Ecker, Sakis Theologis, Sharon Long and, of course, the irrepressible Winslow Briggs. These seminars were my only formal training in plant biology. Sarah was already dedicated to a career in plant biology, and she was determined to go for her post-doc at the Max-Planck-Institute for Plant Breeding in Köln, Germany, then, as now, one of the world's leading plant science centers. I wrote to Klaus Hahlbrock in Freiburg to ask whether he had open positions. He replied, and in another random stroke of luck, he noted that his lab would soon be re-locating to the MPI in Köln. So off to Germany Sarah and I went, and our careers in plant biology began!

What do you consider to be your most important contributions to plant science research?

By far my most important contribution has been to provide a hopefully welcoming and challenging environment for the nearly 100 doctoral and post-doctoral scientists who have enriched and enlivened our lab for the last 32 years. Sarah and I are proud to have collaborated with future Professors, Biotech scientists, devoted teachers, and engaging science journalists who worked in our lab. I try to help people define a risky and creative set of projects, and then we stand at the edge of that cliff, join hands, and jump.

It's not clear how much, if any, of the contributions to our field will still be relevant 10, 50 or 100 years from now, but I do know that for at least the remainder of the careers of our former lab members, some of our 'lab cultural traits' will endure.

We study both the molecular mechanisms of the plant immune system and the intricacies of how that immune system sculpts the well organized and functional root microbiome. Our ultimate aim is to use knowledge, genetics and microbes from nature to enhance plant disease resistance, plant performance and soil sustainability across the globe by defining the fundamental rules of immune system organization and function, and microbiome assembly and function.

I am a primarily a geneticist. We were early developers of Arabidopsis as a genetic and genomic model to define and isolate the genes required for successful immune responses. This led us to isolate and study intracellular NLR (Nod-like) plant immune receptors. These receptors are activated by pathogen-encoded effector proteins. We provided evidence that multiple sequence-unrelated bacterial effectors could activate the same receptor. One model consistent with this genetic result is that the effectors converge onto their nominal cellular target and biochemically perturb it, and the immune receptor monitors the integrity of that target. This became known as 'The Guard Hypothesis', and it has proven to be a major mechanism by which bacterial effectors activate the plant immune system. We provided interactome evidence furthering the idea that a highly diverged class of pathogens converge onto a limited set of host targets. Because cell death is associated with successful immune responses, we isolated auto-immune mutants that mis-regulate cell death. This led us to define 'helper NLRs' that are required for the action of the 'sensor NLRs' that recognize pathogen-encoded effectors.

In about 2007, we shifted half of the lab to the application of reductionist models, like Arabidopsis, to understand how plants sculpted the root-associated microbiome. This has been a challenging set of projects, because we are essentially trying to make ecology a robust experimental topic. We and others demonstrated plants have a structured root microbiome that is at least partially dependent on interaction of root commensals with the plant immune system. We identified a key bacterial genus on the root that is required to enforce auxin homeostasis in complex communities, and we defined plant nutritional responses that repress the immune system to promote microbiome-dependent responses.

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I won't try to list all the lab members with whom we've made these and other breakthroughs possible. However, we have benefited immensely from collaborators and my mentors who have also been instrumental in our success: Roger Innes, Brian Staskawicz, Jeff Ellis, Jonathan Jones, Detlef Weigel, Joe Ecker, Susannah Tringe, Corbin Jones, Paul Schulze-Lefert, Fred Ausubel, Chris Somerville and Jeff Schell; they have been friends and colleagues for over 30 years in most of these cases.

What advice would you offer to a young person contemplating a career in plant science research?

I have actively tried to encounter new experiences, new people, and new ideas. As may be apparent from the description above, random decisions and luck have directed me throughout my career. Omnivorous curiosity is an excellent trait. But luck favors a prepared mind, and I believe that successful scientists are fully committed to digging deep and becoming experts in their own research topic, while being conversant with adjacent fields. In my career, I've been fortunate to change directions at several points. Sharp turns in interest offered the chance to re-capture the curiosity that brought me to science in the first place. Looking for and investigating new directions also helps avoid the crowd. I've tried to avoid the latest trend in the field and have tried instead to define new trends. This means that our work typically was not deep drilling down to the kinase of the kinase of the kinase. Rather, we tried to open new research avenues and populate them with ambitious, dedicated young scientists. As Steve Jobs famously said, "Stay hungry, stay foolish".

I try to develop skills as a problem solver. Methods come and go; sub-disciplines change focus over time. It's always been helpful to me to think of myself not as a plant biologist or immunologist but as a someone who likes to solve puzzles.

I believe it is vital to be generous. Give away your ideas and your reagents freely. Being a lab of open sharers has not led to us being scooped; rather, it facilitates opportunities for new interactions for our students and post-docs. I don't think we ever sent out an MTA (materials transfer agreement) following a reagent request, despite 'rules' to do so set by my employers.

Science is fun. I've tried to stay engaged and passionate. It's easy to accept cynicism as a driving force in a life in science; there are lots of setbacks and seemingly capricious decisions abound. It is harder, but more rewarding, to seek joy and remain optimistic. Science is increasingly a group endeavor and being an active and earnest collaborator is advantageous and makes science more fun. Get to know your cohort in graduate school and in your post-doctoral research—these people will be your friends and mentors for your entire career.

I enjoy being part of a community. There are many diverse careers in plant science, and they will hopefully embed one in a vibrant and motivated community. I am lucky to have been involved not only in ASPB but also in the International Society for Molecular Plant-Microbe Interactions. These organizations provide community, opportunities for service, dedication to international diversity in science and cultural guard rails for our profession. Our profession is quite democratized—peer review of grants and papers are the hallmarks of this—and the general lack of formal structures in science foster bottom-up community building.