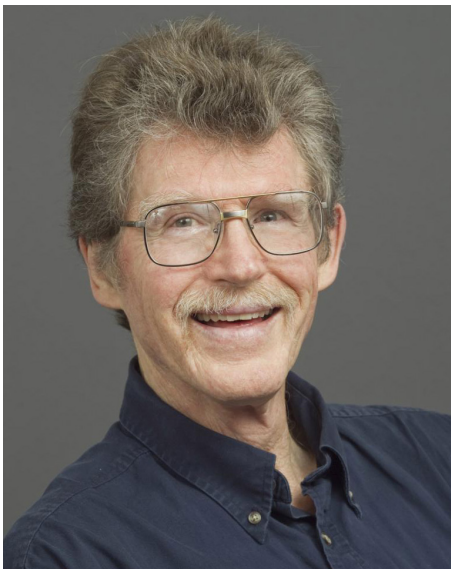
ASPB Pioneer Member

Peter Quail

How did you spend your career and what are your most important contributions to plant sciences?

My path to a research career was a progression of changing objectives, opportunities, and pure luck: Growing up in rural southeastern Australia, I spent a significant amount of time on my uncle's farm. In addition to gaining experience in many aspects of the work activities of farming life (shearing sheep, building fences, harvesting hay, etc.), I used to love to explore, on foot or horseback, the bushland areas on the property. I was fascinated by the native wildlife and flora that existed in that area. Seeing my love for rural life, my parents sent me to a newly established agricultural boarding high school. I had intended, upon graduating from there, to go back to farm life in some undefined way. However, one of my teachers suggested that, given my grades, I should consider going to university, as a degree from there would open the possibility of a career as a farm adviser/consultant. I liked that idea, so in what seemed like a natural progression at the time, I applied successfully for a fellowship and enrolled in a bachelor of Agricultural Sciences degree program at Sydney University with a focus on crop plant growth. The overall goal was to become educated in the latest scientific approaches to agricultural production.



A thunderstorm changed my life. Although this was already the early 60's, Crick and Watson's blockbuster definition of the structure of DNA, together with the burgeoning understanding of how the encoded genetic information was transformed into proteins, had apparently not made it into the curricula of the classes I was taking for my bachelors' degree, because I had never heard of it. One afternoon, after completing my assignment in a zoology lab course, I left to go home. However, when I reached the front door of the building, a thunderstorm struck and there was a torrential downpour of rain. While waiting in the lobby for it to pass, I began reading an article from a Sydney newspaper that someone had tacked on the bulletin board, something I would likely have normally rushed by without looking. It was a layman's description of the central dogma of molecular biology, using the analogy of information stored on a tape-recording, being copied and played to make the molecular product. I was completely mesmerized by the story. This chance experience triggered an intense desire to learn the molecular basis of the growth behavior of cells in the plants that I was studying. This, with the encouragement of two of my undergrad mentors, led to my transitioning into a Ph.D. program at Sydney University after completing my bachelor's degree.

With the broad goal of finding ways to control wild oats, a serious weed of wheat crops, my project soon focused on controlling the dormancy of the oat seed as a potential vulnerable target. In searching the literature on seed germination, I made another pivotal discovery. Joe Varner and colleagues had recently reported their seminal work showing that gibberellic acid could induce cells in isolated barley aluerone layers to synthesize the enzyme alpha amylase, thereby triggering germination. This provided me with an assay I could use to screen oat extracts from contrasting dormant and non-dormant seed sets for potential inhibitors that might impose dormancy by blocking this step in the germination process. Although I never found the silver bullet, I was inspired to try and join Varner's lab at the Plant Research Lab (PRL) at Michigan State University (MSU) for a postdoc.

U.S. postdoctoral experience at the PRL. I was delighted when my application to the PRL was

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accepted. Not being well-informed regarding research institutions in the U.S., I didn't realize I had been lucky enough to stumble upon a premier plant research lab. And indeed, my time there was a truly transformative experience, both scientifically and socially.

Scientifically, I saw for the first time how first-rate science is done. The PRL community was full of bright, lively, interactive faculty, postdocs and graduate students, and participation in daily morning and afternoon coffee breaks in a communal meeting room was strongly encouraged. The discussions and interactions at these gatherings were enormously stimulating and educational for me. Most impactful, however, after working in Varner's lab for a couple of months, I made the most important discovery of my career: I realized I didn't know how to think scientifically. Although I had learned from some wonderful mentors at Sydney University how to do experiments and write, during my PhD studies, I had never been exposed in an overt way to the principle of rigorous, critical thinking. That's what Joe taught me.

Socially, the experience was a personal and political awakening. It was the 60's, and the anti-Vietnam war movement/demonstrations were in full swing. My arrival in the U.S. was the exact week of the Democratic National Convention in Chicago, August 1968. I first stopped in Berkeley for a few days, visiting a friend who was at the university there. There was a dusk-to-dawn curfew, the smell of tear gas was in the air, National Guard troops were stationed at various locations, and all the windows up and down Telegraph Avenue next to the campus had been smashed by demonstrators. I had planned to also have a couple of days in Chicago on the way to MSU in Lansing, Michigan. However, given the news coverage of events there, I simply changed planes at O'Hare airport and flew on through. I had an unforgettable three years in Lansing before heading for Germany.

Germany: Like many young Australians, I wished to travel and experience other countries and cultures before returning home. I also had a long-held desire to learn another language. When, toward the end of my stay at the PRL, I learned of a relatively new institute in Freiburg, Germany under the directorship of Hans Mohr that focused on another of my interests, light-regulated plant responses, this seemed like an ideal opportunity. Moreover, it was located in southern Germany within striking distance of the Swiss Alps, so I would also be able to ski, one of my most beloved activities! I was awarded a von Humboldt Fellowship and, following a two-month submersion course learning German, I was accepted into Mohr's Institute.

Within a short time after arriving in Freiburg in 1971, I became aware of an upcoming NATO-sponsored plant photobiology meeting, in Eretria, Greece, and I was strongly encouraged to go. Once again this was a pivotal experience that would set the direction of my subsequent research path for the rest of my career. That meeting was focused almost exclusively on phytochrome, the only plant sensory photoreceptor that had been identified at that point. It also assembled almost all the major internationally prominent figures in the field in a single relatively secluded location on the Mediterranean for a two-week-plus conference/NATO School. This configuration not only enabled me to get a remarkable introduction to the research field, but also to meet and get to know a large number of the members of this research community.

Also, crucially, during this meeting I got know Dieter Marme and Eberhard Schaefer, two members of a small sub-group of bright, young biophysicists in Mohr's department. They were focused on investigating the *in vivo* dynamics of the phytochrome (phy) molecule, using primarily in-situ spectrophotometry correlated with seedling growth. I could see that combining my biological/biochemical background with their skills had the potential to provide an avenue to begin to probe the, at that time unknown, primary molecular mechanism of phytochrome action in the cell (the holy grail of phytochromology!). Joining them when we returned to Freiburg after the meeting, turned out to be another determinative experience. Through numerous animated discussions, experiments, and white-board lessons, I learned

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the science of photobiology (while also slowly improving my German!). It was a wonderfully stimulating period. This was especially so under the mentorship of Eberhard, who became an enduring, lifelong friend and colleague in the field. These skills were critical in providing the framework for my subsequent research career in photobiology.

Back to Australia and then the U.S.: After returning to Australia in 1973, I spent three years plus as a research scholar in the Research School of Biological Sciences at the Australian National University in Canberra. But I decided to move back to the U.S., where the opportunities for an independent research career were greater. This was made possible by Winslow Briggs, who kindly offered to host me as a senior postdoc in his lab at the Carnegie Institution at Stanford University. Winslow was a wonderful mentor who exemplified civility and professionalism as well as humility, despite his many achievements. While at the Carnegie, I was also extremely fortunate to spend a few weeks in the Nashville, Tennessee lab of Lee Pratt, who I had also met at the meeting in Greece. There, I learned the art of making antibodies and using them to make immunoaffinity columns for purification of the phytochrome molecule, in addition to performing immunoassays. Once more, this period was pivotal in providing the foundation for my subsequent independent research career.

University of Wisconsin, Madison, Wisconsin: After two years in Winslow's lab, in 1979 I was offered a faculty position in the Botany Department at U.W. In my own lab for the first time, the next eight years saw a major shift in the biological sciences research landscape, from which I was most fortunate to benefit. This was the dawn of the molecular biology/genetics-driven dissection of signaling and gene-expression networks in plants. My program benefitted greatly from a combination of factors that included recruitment of a set of highly talented and dedicated graduate students and postdocs, interactions with wonderful colleagues in the plant photobiology and molecular biology communities, rapid advances in the technologies of monoclonal antibody production, cloning, sequencing and expression analysis of genes, and a combination of generous federal grant and biotech start-up funding. In particular I was extremely fortunate to be in the right place at the right time when the newly formed Agrigenetics biotech company established a research hub in Madison and provided collaborative-project funding and technology. With their funding, we were able to establish a monoclonal antibody facility and have our DNA samples sequenced at their in-house sequencing facility. Overall, during that period we defined and characterized the first full-length phy molecule, produced and used anti-phy monoclonal antibodies to map multiple epitopes in the photoreceptor protein, identified a phy deficient mutant in tomato, accomplished the first in-vitro synthesis of the phy apoprotein from mRNA preparations, cloned and sequenced the first phy cDNA and complete gene sequences, and discovered rapid, light-induced, autoregulatory control of phytochrome-gene expression, all driven by a great team of grad students and postdocs.

The ARS/U.C. Berkeley Plant Gene Expression Center (PGEC): In 1987, I was recruited by U.C. Berkeley (UCB) to a faculty position that also involved serving as Research Director of the PGEC. I remained in that position for the remainder of my career. The PGEC, a newly established research center designed by Gerry Still, a USDA/Agricultural Research Service (ARS) scientist, is a collaborative effort between the ARS and UCB. This design combined the resources and personnel of the ARS with those of the Plant and Microbial Biology (PMB) department at UCB.

The initial phases of this new opportunity coincided with a very exciting time in plant science, during which the field of molecular biology was evolving at a rapidly accelerating pace. The molecular tools for cloning and sequencing plant genes and their cDNA products were becoming more readily accessible, protein-interaction screens of libraries became available, Arabidopsis was emerging as the preeminent model system for molecular genetics and genomics, increasingly facile Agrobacterium-mediated plant transformation and T-DNA insertional mutagenesis all

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became widely available, and ultimately the Arabidopsis genome was sequenced.

These and other developments made possible another series of major advances in my lab that defined some of the core questions in light signaling through the phy photosensory system. As before, this work was done by a series of extremely talented and dedicated graduate students, postdocs, and my long-term lab manager and colleague, Jim Tepperman. Moreover, once again, in addition to the generous ARS annual funding provided with the PGEC position and the federal competitive grants I had at that time, I was fortunate to benefit from another infusion of support in the late 1990's in the form of a collaborative research agreement between the Novartis (later Syngenta) Torrey Mesa Research Institute and the UC Berkeley PMB department.

Soon after moving to the PGEC, we discovered that Arabidopsis has not one, but a small family of five phytochromes (phyA,B,C,D and E), and we cloned and sequenced three of them. Subsequently, we and others went on to show that these phys share both overlapping and distinctive molecular and functional activities in the living plant. Although it was well established by that time that the phys regulate gene expression in response to light signals, the nature and components of the intervening signaling pathway remained unknown. Defining this pathway was my long-held passion. In our first Yeast-2-Hybrid screen of an Arabidopsis cDNA library for phy-interacting signaling partners, we identified a bHLH transcription factor (that we called PIF3) that bound to the phy molecule, specifically in its photoactivated Pfr form. This was a truly exciting discovery, because contemporaneously Akira Nagatani's lab in Japan had shown that light induces rapid phyB translocation into the nucleus. Together, these findings strongly suggested that the signaling pathway from light-activated phy to photoresponsive target genes was extremely short and direct. This basic conclusion was borne out and elaborated in numerous studies from my own and many other labs over the following two decades. This was a paradigm shift in the field.

Subsequently, we identified multiple PIFs (members of a small bHLH sub-family), and eventually succeeded in defining a biochemical mechanism of signal transfer at the phy-PIF interface. We found that the light-induced binding of phyB to PIF3 triggers rapid phosphorylation, ubiquitination, and degradation of the transcription factor, leading to reduced expression of target genes. We also identified the protein kinases and E3 ubiquitin ligases involved in this process.

In an early, parallel, genetic approach to identifying signaling pathway components, postdoc Xing Wang Deng identified and cloned a locus we called *CONSTITUTIVE PHOTOMORPHOGENIC 1 (COP1)*. For this, we used a screen of a T-DNA-insertion library for Arabidopsis mutants displaying a seedling de-etiolation phenotype when grown in darkness. This initiated a line of research that identified COP1, SPA1 and other functionally related proteins as components of the ubiquitin proteasome (UPS) pathway. These and subsequent data from other labs provided evidence of a new mechanism of light-regulated development by demonstrating that regulated protein degradation functions in sustaining skotomorphogenesis in the dark.

Over time, increasing dissection of the phy-PIF signaling module by multiple labs revealed entrancing complexity, both within the module and the transcriptional network it controls. We and others found that each of the individual phytochrome and PIF-family members have both overlapping and distinctive sensory and regulatory roles, combinatorially providing a montage of gene expression and phenotypic outputs. We also found that of the hundreds of genes bound and regulated by the PIF transcription factors (direct-target genes of the PIFs), a significant fraction themselves encode a variety of transcription factors, positioning them to pleiotropically regulate a cascade of diverse downstream cellular pathways.

Superimposed on this complexity, the PIFs have emerged (from the work of many labs) as a multifunctional hub, serving as a convergence point for transcriptional regulation by an array of endogenous regulatory signals, including hormones (GA, BR's, auxin, ABA, ethylene, JA) and the

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circadian clock. Recently we found the circadian clock connects directly to the PIFs through the binding of multiple, integral, central-oscillator components (the PRR proteins) to the transcription factors, thereby modulating the PIF-regulated transcriptional network.

In conclusion: As I said in a previous biography: "I am deeply indebted to my superb mentors, Joe Varner and Winslow Briggs, who nurtured my passion for science, while teaching me the power and necessity of rigorous, critical thinking and professionalism, and I believe strongly that I have a central obligation to pass these values on to those trained in my lab. Indeed, I have been exceedingly fortunate in having some of the most talented, dedicated, and hard-working graduate students, postdocs and technicians as coworkers that one could ever hope for. Several of them have gone on to establish high profile research programs in their own right. I hope my credo of trying to promulgate the highest standards of scientific rigor and critical research thinking has contributed, at least in part, to their success."

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

As outlined above, I would say my contributions to defining the primary molecular mechanism of phytochrome action are the most important, scientifically. On the other hand, the contribution that I feel most proud of is my participation on the Scientific Advisory Committee of the Rockefeller Foundation's International Rice Biotechnology Program (1990-2000), which was led by Gary Toenniessen. This highly successful program leveraged the scientific excellence and existing funding and infrastructure available at advanced institutions to launch the fundamental molecular genetic technologies necessary to establish the foundation of the rice biotech program, while simultaneously training young scientists from, and establishing strong scientific linkages with, research communities in developing nations.

When did you become an ASPP/ASPB member?

I don't recall exactly, but I think it was sometime between 1968 and 1971.

How did the society impact your career?

In multiple ways. I became a member of an organization and community that shared the same broad common scientific interests and goals and provided a network of knowledge and experience from which I have benefited greatly. The journals, Plant Physiology and Plant Cell, have not only provided an avenue for our own publishing, but are an important ongoing source of information on advances in the field, both scientifically and technologically. The annual meetings have provided an excellent opportunity to present and hear the latest advances, not only in my own field, but also areas outside my research focus, especially at the mini-symposia. I have found them especially informative and useful for hearing about new technologies, approaches and techniques. They have also provided an ideal opportunity to establish connections and collaborations, as well as to meet up with old friends and colleagues and meet new ones. Similarly, they have provided a venue for my grad students and postdocs to get experience in presenting their work and begin to establish the networks that are so important for their development as scientists.

What important advice would you give individuals at the start of their career in plant sciences?

Follow your passion. But don't become fixated on a single idea or hypothesis. Remain flexible and open-minded. Try to always follow the principles of Strong Inference (J.R. Platt (1964)): 'You can never *prove* a hypothesis; only *disprove* it.' Learn to critically evaluate your own work. Become the toughest critic of your own work. Don't be afraid to say that you don't know something. Remain curious. Seek out and have as many discussions with colleagues as you can. 'Other people have had some of my best ideas'. Practice giving oral presentations at every opportunity. Practice writing: it's a continuing quest. When you get your own lab: Have an open-door policy for your lab members to drop in at any time. Encourage them to learn and be open to the power of critical thinking.