Dean DellaPenna

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

My path to becoming a research scientist and professor was anything but direct, planned, or predictable. I grew up in a small town in the Ohio Valley, where the primary industry was steel. After graduating from high school, I lacked not only the money but also the motivation and discipline for college, so I got a job in the local steel mill and was assigned to the coke plant. Coke plants are where mountains of coal are unloaded from river barges, moved, mixed, and baked to generate coke to fire the mill's blast furnaces. In addition to coke, the massive ovens continuously generate copious amounts of heat and sulfur gas, so it was literally like working in hell! Two years of this provided me all the motivation and some of the money I needed to enter Ohio University in the Fall quarter of 1980, at age 21, as what we now call a "non-traditional" student. As the first member of my family to go to college, I received loads of encouragement but very little practical guidance.

A college advisor suggested I try business as a major, and after my first two economics courses I understood why it is called "the dismal science": it annoyingly fails to predict what the economy does, would do, and why. Thankfully, I was rescued from this fate by an elective in spring quarter, Botany 101, taught by Dr. Larry Larson, whom I credit with sparking my interest in all things plant. Here at last was a subject where things made sense to me, were predictable, testable and to my delight the more molecular I went the more sense things made. I was hooked. Beginning my second year I devoured all the science courses I could, graduating with a BS in Botanical Cell Biology, a major requiring so much biology and chemistry no one had ever taken it! Hooked indeed! I also qualified for work study my sophomore year and eventually found my way to the plant research building, which proved pivotal. I quickly mastered routine lab maintenance tasks and then got to participate in experiments studying the uptake of sulfate into cultured tobacco cells. From this I learned experimental design, the scientific method, the importance of controls, protein purification techniques and how to organize my time to maximize both classroom learning and experiments. While these were all important steps in my scientific development, I now recognize the most critical was that I became sufficiently comfortable with my work study professors to ask for career advice. I have done all I can in my own career to pay this forward, especially for first generation college students like myself.

As graduation approached, I had no idea what came next, only that I loved doing experimental science and desperately wanted it to continue. My work study professors suggested I apply to graduate schools...something that had never crossed my mind as an option! I ended up at UC Davis in the lab of Alan Bennet who gave me a thesis project to purify and clone a gene encoding a cell wall enzyme in ripening tomato fruit and the room to work at my own pace, which I did at breakneck speed, publishing several papers while in his lab. In addition to earning my PhD in graduate school, I taught myself to tie flies and fly fish; as anyone who knows me will attest, fishing has been a favored diversion since childhood. While at Davis, I collaborated and became good friends with Jim Giovannoni, a fellow graduate student working on tomato fruit ripening at Berkeley. In addition to a productive scientific collaboration, we discovered we both had the fishing disease and have continued to collaborate on fishing outings the past 35 years, including nine Alaskan fishing trips.

After Davis, I was set to continue working on tomato as a postdoc with Bud Ryan at Washington State University, but I first made

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a 3-month detour to Auckland, New Zealand, where I was invited by a UC Davis alum to teach a molecular biology course and do molecular work on ripening apples. My time there was productive on many fronts. Predictably, I enjoyed several long weekends of memorable flyfishing in New Zealand's lakes and streams and published a small paper on ripening apple molecular biology, but perhaps the most important thing was I spent 2-3 hours a day in their quiet, well-stocked science library, browsing the stacks and voraciously reading more broadly and deeply than I ever had. I came back to the US with pictures of beautiful scenery and trout and a head full of ideas for future work.

My postdoc at Washington State was relatively short, as I was hired as an assistant professor in the Plant Sciences Department at the University of Arizona in 1990 and received a grant funded by NSF to continue my work on tomato cell wall enzymes. I also initiated a genetic approach to isolate carotenoid biosynthetic enzymes using existing tomato fruit color mutants, as my reading in New Zealand had convinced me these were interesting compounds and that genetics was going to be the best route to cloning the challenging enzymes that made them. In 1993, as I entered my third year as an assistant professor, I had two important realizations that set the tone and direction of my research for decades to come. The first was that progress on cell walls was going be agonizingly slow for the foreseeable future due to technological limitations in cell wall analytics. The second was that despite having generated mapping populations for several tomato fruit color mutants, the map-based cloning in tomato I envisioned was also not likely to be feasible for some time. At this point, serendipity played a role, as another recent Arizona hire, Ken Feldman, was across the hall from me and working exclusively on Arabidopsis. The more I read and thought about it, the more convinced I became Arabidopsis would be the most tractable system for my near- and mid-term research goals. I made the naïve/gutsy/insane decision to phase out working on cell walls and tomato to focus on genetically dissecting carotenoid synthesis in Arabidopsis, an organism and research topic with which I had no experience. I did so by trusting my reading and gut, but it was certainly not obvious at that time that this was a wise decision. It is only with the benefit hindsight I can say that it really was.

I settled on two parallel approaches to identifying carotenoid pathway mutations: for early pathway steps, HPLC analysis of tissue culture grown T-DNA lines segregating for (soil lethal) pigment-deficient phenotypes, and for mutations affecting later pathway steps, brute force HPLC based screening of a soil grown, EMS-mutagenized population, as my interpretation of the literature had convinced me (but not grant reviewers) that such mutants would not be lethal. We failed to identify carotenoid mutants in first 1000 EMS mutants, a deeply unsettling outcome that caused a hard reassessment of the underlying logic, which I concluded was still valid. In the next 1000 EMS lines, several mutants were isolated, including those that, in two 1996 publications, would define the biosynthesis of lutein, the most abundant xanthophyll in photosynthetic tissue. These and other xanthophyll mutants, singly and in combination, were used over the next decade to understand the functional role of specific xanthophylls in photosystems and LHCs and later to manipulate the pathway in seeds, where the mutations had strikingly different phenotypes from leaves.

From tissue culture screening we identified two, non-allelic mutant lines segregating for albino seeds that accumulated phytoene, the first compound of the carotenoid pathway. That neither mutation mapped to phytoene desaturase indicated the reaction required three gene products, stressing for me the power of this genetic approach. Both mutants disrupted plastoquinone (PQ) synthesis, genetically defining it as the electron acceptor for phytoene desaturation. One mutant could be chemically complemented with homogentisic acid, from which the aromatic head group of PQ is derived, indicating it likely disrupted the enzyme producing it, the gene of which had not been cloned from plants. A new Arabidopsis resource, Expressed Sequence Tags (ESTs), fundamentally changed our approach to cloning. ESTs are randomly selected, hypothesis-free

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cDNAs subject to single pass Sanger sequencing and these data were deposited into a publicly accessible database. A BlastP (protein to protein) search of the database with a human ortholog identified a single truncated Arabidopsis EST with 17-27% protein identity to human, bacterial, and fungal orthologs. Significantly, the EST had insufficient DNA identity to detect by nucleotide-based searches with these orthologs. This approach was a revelation and allowed us to identify and characterize the Arabidopsis ortholog and underlying mutation more rapidly than I ever imagined possible. This work took place in the mid-1990s, long before plant genome sequences became available, and it drove home at an early stage of my career the power large-scale DNA sequencing resources had for plant metabolism research, a lesson I would apply repeatedly throughout my career. A fortuitous side product of this work was that the identified enzyme not only formed the head group of PQ but also that of tocopherols (vitamin E), which launched a major new research program in my lab to dissect tocopherol synthesis and function in plants.

Concomitant with this work, in 1996 the first cyanobacterial genome, Synechocystis PCC6803, was published. Like plants, Synechocystis also makes tocopherols and though I had never worked with it, I thought it could prove useful in dissecting the pathway. A BlastP search with the Arabidopsis aromatic head group sequence identified a single Synechocystis ortholog with 35% protein identity that was present in an 11 gene operon. One of the other genes in the operon had methyltransferase protein motifs, and because bacteria organize pathways in operons and two enzymes in the plant tocopherol pathway were methyltransferases, we targeted it for functional analysis. Unlike Arabidopsis, homologous recombination is possible in Synechocystis and targeted disruption of this methyltransferase resulted in loss of a-tocopherol and accumulation of its biosynthetic precursor, g-tocopherol. An Arabidopsis methyltransferase ortholog was obtained from the EST database and when overexpressed in Arabidopsis seeds, which normally accumulate 95% g-tocopherol, resulted in its complete conversion to a-tocopherol. This small change, addition of a single methyl group, has large consequences for human health, as it increases vitamin E activity 10-fold relative to g-tocopherol. This work helped crystalize for me the concept of Nutritional Genomics, the use of genomics writ large to target areas of plant metabolism that are beneficial to human health. This is especially true for micronutrients, whose dietary deficiency is a major global health problem, primarily because the seeds of major global staple crops, the plant tissue most abundantly consumed by humans, have insufficient levels of most micronutrients to meet daily requirements. I presented our tocopherol work and the general concept of Nutritional Genomics to an enthusiastic audience at the 1998 ASPB meeting in Madison, Wisconsin.

I've spent the majority of this biography focusing on the early portion of my career - up to 1998, as I thought my reflection on this period in particular might be most useful for any students or early career scientists who read this; it certainly would have been for me! In the decades that followed, my lab and others around the world have continued to dissect, manipulate and engineer the tocopherol and carotenoid pathways in plants and push forward the idea and reality of Nutritional Genomics. By the mid 2000's, both pathways had been fully elucidated, but efforts to engineer and/or breed for a given metabolic outcome often gave unpredicted results, especially in seeds. I again turned to genetics to determine the molecular basis of natural variation for these traits with the simple idea that understanding how Mother Nature increased a given compound might provide insight into the reason(s) for unexpected engineering/breeding results with pathway genes. Publication of the Arabidopsis genome in 2000 defined the genomic positions of all known pathway genes and allowed us to ask a relatively simple question: How many of the QTL for our traits in seeds have known (and therefore potentially causal) pathway genes in their intervals? The answer surprised me: ~75% of QTL lacked known pathway genes in their intervals and these novel QTL often had effects larger than QTL intervals containing pathway genes! With so much information missing, it became clear why engineering

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with just pathway genes often had limited success. This result set my group on a more than decade long effort of using QTL and genome wide association studies to identify, isolate and functionally characterize novel, large effect loci for these traits in Arabidopsis seeds and maize grain. Our ongoing efforts are highly collaborative undertakings with colleagues on the MSU campus and across the US, without whose expertise and technical knowledge in their specialty areas would simply not make this research possible. The driver for all these collaborators is that, in addition to being cutting edge science, a better understanding of how micronutrient levels are controlled in plants in general, and in the edible portions of global staple crops in particular, is vitally important research for humanity. We've recently published two papers in Plant Cell that lay out the most comprehensive genomic and genetic roadmaps for engineering, breeding or a combination of the two, to realize this goal for tocopherols and carotenoids in maize kernels and likely seeds of other major row crops. Currently, the group has turned its efforts to specific B-vitamins, which are also limiting in the seeds of most staple crops.

When did you become an ASPB member?

This happened as a graduate student in 1986 (pre-online journal days), so I could receive and read Plant Physiology (and later Plant Cell) issues as soon as possible.

How did the society impact your career?

At all levels, the society has, through both its journals and talks and posters at annual meetings, provided me and my lab members the ideal venue to convey our work to the most appropriate global community. The society has also been instrumental in the continuing education of myself and my lab members on topics, technologies, and approaches outside my lab's areas of expertise. By enabling my interactions with scientists at all stages their and my career, ASPB meetings have been key to my scientific development and for initiating many of my most productive and enjoyable collaborations. I vividly remember my first ASPB meeting and poster and how kind and welcoming the existing Society members were, and continue to be, to its newest members. Finally, from a personal perspective, ASPB meetings continue to provide the best opportunities to catch up with and enjoy the company (and science) of many wonderful colleagues, collaborators, and friends who I would otherwise rarely get to see.

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

Everyone reads deeply in their immediate research field, especially when grant, paper or thesis writing, but just as important to long term success is to routinely prioritize a few quiet hours each week to read and think deeply about papers/topics/approaches outside of your immediate research area. My experience is that this type of reading is often where some of your better ideas come from. Always trust your own instincts in your research, but also be the harshest critic of your writing, thinking and logic and work to continuously improve and refine each of them. At every stage of your career take every opportunity to present your work orally, but treat each talk as if it were a job interview, because sometimes it might be without your knowing it. Finally, try to remember each key act of kindness, encouragement and advice you've received at every stage of your education and career, and try to give as good as you've gotten as you proceed through your own career.

Academic Family Tree
https://academictree.org/cellbio/tree.php?pid=655721