ASPB Pioneer Member

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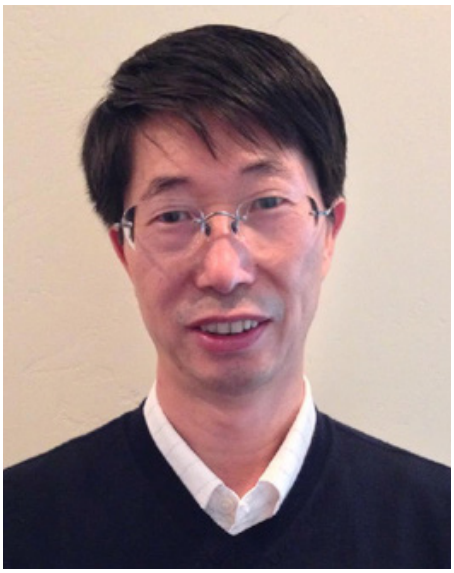
How I spent my career.

I grew up in a small fishing village on the Southeast coast of China, during the Cultural Revolution. Three profound memories of my childhood, together with a lot of luck, shaped my life and my career: the hunger I suffered day to day, the beautiful coastal nature of my surroundings, and the witness of my neighborhood teacher being captivated in the darkness of a ruined classroom. To escape from the hunger, I dreamed to enter a college/university, the only way for a country boy to leave the impoverished countryside back then. My luck came as the Cultural Revolution ended when I was in high school, which coincided with the resumption of competition-based college enrollment in China. I left my village for the first time in 1978, at the age of 17, to attend the South China College of Tropical Crops (currently merged into Hainan University) on the Hainan Island.

The dark experience of my childhood precluded me from considering a major in the social sciences in college. My aspiration to search for answers to scientific unknowns came from the popular science books I read as a child. Books were hard to find in the China countryside back then, but I was able to borrow a popular science series for children entitled "100,000 WHYs" from my neighbor. I was glued to these books and finished reading them in



one day. I was captivated by what nature presents and how scientists discover the underlying principles for natural occurrences. From then on, I dreamt of exploring the mysteries behind the fascinating nature that surrounds us all. Frustrations and difficulties have sometimes triggered thoughts of pursuing other career paths, but my heart has always pulled me back to science. The thought of solving a scientific mystery can pump up my adrenaline and make me forget about scientific manuscript rejections, grant denials and other frustrations.

My undergraduate major was crop pest management, which I thought would help alleviate hunger in human beings. But I soon realized that pest management involved very descriptive work that failed to excite me and was not in line with my childhood dream of exploring the unknown principles of natural occurrences. Luckily, upon my graduation I was awarded a fellowship to pursue graduate studies in the United States, where I wanted to study the physiological and biochemical basis of pathogenesis and defense against plant pathogens. However, a college administrator at the South China College of Tropical Crops denied me this golden opportunity; he insisted I must study disease management. For the first time, I realized that I was naïve to think I could escape politics by focusing on my scientific passion. But I learned I would have total freedom to choose what I studied once I was in US. After agreeing to the administrator's demand, I went to the laboratory of Dr. Charles Martinson, who studied both maize disease management and physiology at Iowa State University. A seminar by Noel Keen (an ISU alumnus) inspired my interest in the molecular mechanisms of plant-microbe interactions.

After obtaining a MS degree at ISU, I joined a Ph.D. program on molecular plant pathology at Virginia Tech and worked under the direction of both George H Lacy (a bacteriologist) and Carole Cramer (a plant molecular biologist) on the molecular interactions between potato tubers and the bacterium *Erwinia carotovora*, which causes soft rots in potato tubers and other stored vegetables. My focus was regulation of the genes encoding cell wall degrading enzymes as key pathogenic factors. My naïve thinking was that Erwinia, a close relative of *E. coli*, was an easy system to investigate and soon no major

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unknowns would exist. For my postdoctoral training I decided to move to more complex systems: signaling mechanisms in plants. This was essentially a completely unexplored field. In 1990, I joined John Watson's group at the University of Maryland (College Park) to work on blue light signaling in pea. After more than two years of frustrations and failures in the attempt to determine how blue light regulates gene transcription in pea, I was depressed and considered quitting plant science. However, my heart would not let me do it, and I decided to read extensively in the library and search for other significant and exciting questions in plant biology. Reading about exciting research findings helped relieve my depression. One of the exciting findings was the identification of genes by John Pringle's and other groups that encode a very conserved Rho small GTPase, CDC42, that regulates establishment of cell polarity in yeast. This triggered my realization that cell polarity, a completely unexplored field in plant biology at that time, must be of paramount importance in plant development. It led to my interest in cloning the Rho GTPase homologs in plants, ROPs (Rho-like GTPases of plants). My subsequent investigations of ROP-based signaling mechanisms that regulate the cytoskeleton, cell polarization, polar cell growth, and cell morphogenesis in plants followed.

While I was still a postdoc at UMD, Carol Cramer and I submitted an NSF grant proposal, and we were extremely lucky to receive the award. As the grant was submitted via Virginia Tech, I moved back there as a research scientist in 1993. I was successful in obtaining another grant, this one from the USDA, before I became an Assistant Professor at Ohio State University in 1994. In my own laboratory, I used two model systems in Arabidopsis (growth of pollen tubes and formation of leaf pavement cells) to investigate signaling mechanisms underlying creation of cell polarity, tip growth, and cell-cell coordination of morphogenesis. My decision to work on cell polarity and obtain grants as a postdoc was essential for me to secure a faculty position in an extremely competitive job market. My next big decision was to move to the University of California at Riverside in 1999. For several reasons this move boosted my research to the next level. First, I was surrounded by extremely supportive colleagues, including Elizabeth Lord, Julia Bailey-Serres and Anthony Huang. Second, a couple of years after I joined UCR, Natasha Raikhel was hired and established the Center for Plant Cell Biology (CEPCEB). Natasha created a first-class infrastructure and a stimulating and collegial environment in which plant cell biological research blossomed. Third, Natasha's leadership and an outstanding cohort of colleagues provided me with unparalleled support and a stimulating intellectual environment. Last but not the least, I had the good fortune to be associated with a group of super and collaborative postdocs and graduate students, among whom many now have a successful academic career of their own.

I am not a hero, but an old Chinese saying "times make a hero" could not have been more accurate for my chosen research area. The timing for me to get into mechanistic studies of cell polarity was perfect. When I identified ROPs, my first intuition was that I needed a biologically interesting but technically easily manipulated system that is amenable to molecular, genetic and cell biological analyses to study the mechanisms underlying formation of cell polarity in plants. At that time, there were no molecular studies of cell polarity in any plant system, so I had all systems to choose from. The question was which one. I considered the elegant *Fucus* zygote, where Ralph Quatrano had done beautiful physiological studies of cell polarity regulation, but it is not amenable to molecular genetic analyses. My luck and the beauty of the nature helped. A western blot analysis showed me that ROP proteins are highly abundant in pollen. Consequently, I decided the tip-growing pollen tube was the best system for studying apical cell polarity in plants. As a culturable "single cell" with a haploid genome, it is basically the "yeast system" in higher plants. Immunostaining revealed the distribution of ROPs in pollen tube tips, demonstrating the first plant proteins shown to

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be polarly localized; we subsequently applied various reverse and forward genetic methods and molecular and cell biological tools to investigate the Arabidopsis pollen tube system.

After setting up the pollen tube system, serendipity introduced me to another fascinating system: the puzzle piece-shaped leaf epidermal pavement cells with their interdigitated lobes and indentations. We wanted to probe the function of ROP2, which is expressed throughout various vegetative tissues, by constitutively expressing active (CA) and dominant negative (DN) mutants of ROP2 in Arabidopsis under control of the CaMV 35S promoter. When my graduate student, Hai Li, showed me images of wild type pavement cells and those in CA-rop2 and DN-rop2 transgenic plants, I was so intrigued by the amazing cell shapes that I immediately decided pavement cells would be an excellent system for studying the mechanisms underlying formation of cell polarity and shape in a multicellular plant tissue.

In the 1990s, there was some description of cellulose deposition patterns associated with the arrangement of microtubules in pavement cells, but no molecular or genetic studies had been reported on pavement cell formation. Hence, the pavement cell system came under my radar with excellent timing. ROP2 provided a stepping-stone for us to investigate the molecular mechanisms underlying formation of their puzzle piece shape. At that time, however, I had no idea this interesting system for cell biological studies would later become an excellent model system for discovering the role for auxin regulation of cell morphogenesis and a new auxin signaling system on the cell surface.

Timing is not everything. As mentioned above, the unlimited support from Natasha Raikhel, the outstanding infrastructure she built, and the stimulating and collegial environment at CEPCEB was instrumental in the trajectory of my career, as were the many excellent graduate students and postdocs with whom I was fortunate to be associated. I was not a cell biologist by training, but I learned how to stand on the shoulder of giants. I had several postdocs, including Junko Katsuda, Yakang Lin and most importantly Ying Fu, who were super talented and very well trained in microscopy and imaging. They taught me cell biological and microscopy knowledge and trained other postdocs and graduate students in these arts.

What do you consider your most important contribution to plant science?

After establishing the Arabidopsis pollen tube and pavement cell systems for investigating the molecular mechanisms responsible for formation of cell polarity, tip growth and cell morphogenesis in plants, my group made several contributions that are worth mentioning. First, we uncovered a ROP-based signaling network regulating tip growth in pollen tubes, which involves dynamic activation of ROPs at the cell apex, two opposing ROP signaling pathways regulating actin dynamics and exocytosis, and feedforward and feedback loops that contribute to the ROP activity dynamic and oscillation at the pollen tube apex. Second, by integrating computational modeling with experimentation, we showed that an exocytosis-coordinated mechanism provides a minimal design principle for tip growth and overarches the regulation of rapid tip growth, growth guidance, and cell wall maintenance under mechanical stress. Third, we elucidated a CrRLK1L-dependent ROP signaling pathway that senses mechanical stress experienced by pollen tubes growing from the stigma to the transmitting tract. Similar pathways may also regulate mechanical responses in other plant cell systems, such as pavement cells.

In the area of pavement cells, we also uncovered a signaling network composed of two mutually inhibiting ROP signaling pathways that regulate the formation of puzzle-piece shapes. We showed that these pathways are activated by auxin, and we provided evidence that auxin not only activates the two pathways within a pavement cell, but also coordinates the activation of these pathways across adjacent neighboring cells. Importantly, these studies led to the discovery of cell surface-based auxin signaling

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pathways, involving a receptor-like kinase known as TMK, that are emerging as a crucial auxin signaling mechanism to coordinate with the well-known TIR1/AFB nuclear auxin signaling pathways. Recent findings demonstrated that auxin induces the formation of sterol lipid-protein nanoclusters that are composed of TMKs and ROP6 and play a critical role in establishment of the cell polarity needed for the puzzle piece shape formation. We demonstrated that auxin-activated TMKs directly interact with, phosphorylate, and activate a plasma membrane proton ATPase causing cell wall acidification, explaining the 50 year-old acid growth theory. As shown for pollen tube tip growth , this latest finding suggests ROP signaling pathways integrate other signals, such as cell wall pectin and mechanical stress, in regulation of cell shape formation in multicellular tissues.

What advice would you offer a young person considering a career in plant science?

When my postdoctoral research didn't go well, I thought about moving into a mammalian system that had immediate medical implications. But after months of soul searching, I realized my passion was in plant science. There are many unsolved mysteries in the plant world that are not only directly linked to food and nutritional needs but also relevant to medical sciences. Once you find your passion in plant science, identify an important and significant outstanding question that you would like to explore during your career. Think big and visionary. Create your own niche and dig into it. You can find undiscovered gold mines. Avoid research questions being addressed by big labs. Always embrace new technologies.

For a graduate student interested in an academic career, productive Ph.D. dissertation research is very important, as this will help you to land a postdoc in a top lab. Having postdoctoral experience in a highly reputable and productive lab cannot be overemphasized. Excellent pedigrees are usually associated with great minds, outstanding research environments, effective mentorship, and resources, and so on. However, there are plenty of examples of scientists who did well in their scientific career without a fabulous pedigree, but only if they were lucky enough to have had supportive mentors and possessed the key attributes of good scientists: aspiration, dedication, vision, creativity, diligence, persistence, and an understanding of the perks associated with a good research pedigree and consciously acquired or gained access to it.

I was very lucky to have been associated with several important and supportive mentors throughout my graduate studies, postdoctoral training, and career. My Ph.D. co-advisor, Carole Cramer, was a scientific aspiration to me. She is a very smart and extremely dedicated scientist. She has two children and a professorial husband, and she runs a successful research laboratory and a startup company. I will never forget the time she and I worked together until 4:00 AM on an NSF proposal. My other Ph.D. co-advisor, George Lacy, was a father-figure and mentor who taught me the importance of securing a competitive grant before landing a faculty job. Owing to his advice, I obtained an NSF grant, a critical factor to secure a faculty position for someone lacking a glorious pedigree, especially in difficult times when there were only few positions available. John Watson, my postdoctoral advisor, was one of the most supportive mentors one can have. While he had a small laboratory, he gave me the freedom to conduct independent research projects to take with me, which was another key factor contributing to my success in landing a faculty position during difficult circumstances. Last but not least, Natasha Raikhel, one of the most supportive colleagues I have known. Since the time I met her in 1995, she has provided and continues to provide me instrumental mentorship.