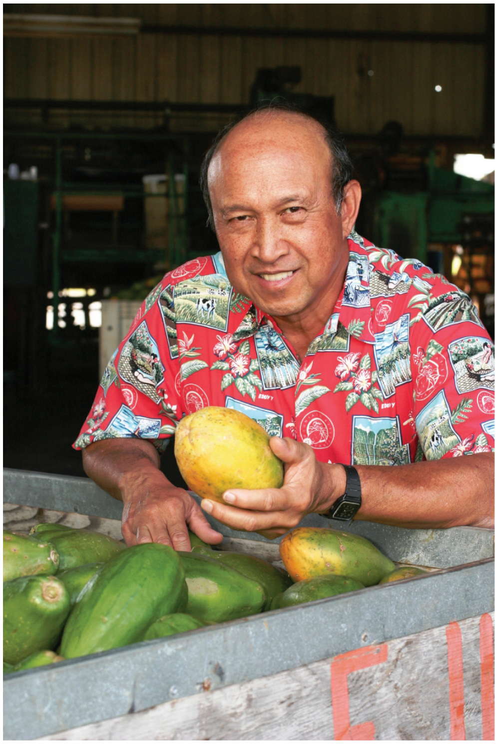

The Wayward Hawaiian Boy Returns Home

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Abstract

This chapter represents a travelog of my life and career and the philosophical points I acquired along the way. I was born on a sugar plantation on the island of Hawaii and early on had a stuttering problem. I attended the Kamehameha Schools and received my BS and MS degrees from the University of Hawaii and my Ph.D. from the University of California at Davis. I link my life and career to various principles and events, some of which are: the importance of positioning oneself; going for the big enchilada; music, the international language; the red zone of biotechnology; the human side of biotechnology; the transgenic papaya story; and my leadership time at USDA in Hawaii. The guiding light throughout my career were the words from Drs. Eduardo Trujillo and Robert Shepherd, respectively, "Dennis, don't just be a test tube scientist, do something to help people" and "Now tell me, what have you really accomplished?"

INTRODUCTION

I felt very honored to receive the invitation to write the prefatory review for the *Annual Review of Phytopathology*. As I reread the letter, the sentences "Our readers generally seek out this particular chapter to help understand the various paths that can be taken to leadership in our discipline" and "Please share your life and thoughts with our readers" caught my attention because they reminded me of a talk I gave to the Kohala Senior Citizens group about my career since I left Kohala and roamed the mainland United States. The talk was enlightening to many of the audience because they remembered me as the barefoot kid from the sugar plantation camp. Similarly, this discourse is a travelog of my life and career as a plant pathologist and interspersed throughout are lessons and philosophical points that I picked up along the way. I present this chapter in story form because it forces one, I believe, to make things simple and homey and hopefully more interesting.

LIFE ON THE SUGAR PLANTATION: STUTTERING AFFECTS MY PERSONALITY

I was born and raised on a sugar plantation in North Kohala, the beautiful and windy rural northern tip of the island of Hawaii that faces the island of Maui. We lived on the Halaula sugar plantation camp where my dad worked for the Kohala Sugar Company, which was owned by Castle and Cook, Inc. Sugar was the only thing in town. I would say 90% of the families were associated with sugar. My father was born in Kohala to Portuguese parents who had emigrated from the Azores and the Madeira Islands. My mom was also born in Kohala to a father who had emigrated from southern China and a mother who was a full-blooded Hawaiian. My family was not ethnically unique, and we intermingled with kids that were commonly of mixed Filipino, Japanese, Chinese, Puerto Rican, Portuguese, Japanese, or Korean ancestry. We did not interact much with the plantation managerial families, as they lived in their own camp and most of them were Caucasians from the mainland United States.

As a youth, my passion was baseball and Ted Williams of the Boston Red Sox was my hero. Halaula had one baseball field where we kids played and where the workers played softball in the plantation league. My friends and I came from the same economic status; we were not rich but had sufficient food from our home gardens and the staples that were bought from the company stores. We enjoyed a carefree childhood and attended the one room per class Halaula elementary public school. It taught us adequately.

Stuttering was my biggest handicap. It was not so much that I stuttered my words, but as I spoke and thought of the next word to say I would often have a psychological block and I would say "um um um" before I could stammer out the word. Naturally, I was a very poor reader when the teacher had us read passages out loud from a story. I had no problem on the ball field, no problem singing, but a huge problem speaking before people. It affected me to the point where I would not volunteer to speak or ask questions in the classroom.

ADMISSION TO KAMEHAMEHA SCHOOLS: IMPORTANCE OF POSITIONING ONESELF

The Kingdom of Hawaii was formed in 1810, 32 years after Captain Cook discovered the Hawaiian Islands, when Kamehameha, the chief of Hawaii Island, united the islands of Hawaii, Maui, Lanai, Kahoolawe, Molokai, Oahu, Kauai and Niihau (31).

King Kamehameha the Great died in 1819, a year before the first congregational missionaries arrived in Hawaii from New England. In the ensuing years, with the advent of sugar cane and pineapple plantations, commerce, and the lure of Hawaii as a paradise, the Kingdom of Hawaii became very prosperous. However, diseases and other factors had ravaged the native Hawaiian population, bringing their population down to approximately 44,000 (of a total population of about 80,000) in 1884, as compared with a population of approximately 300,000 in 1778 when Captain Cook discovered the Hawaiian Islands (48). Furthermore, many native Hawaiians were not able to adapt to the changing lifestyle imposed by the newcomers to Hawaii.

Perhaps seeing the impending demise of the Hawaiian race, in 1884 Princess Pauahi Bishop, who was a direct descendent of King Kamehameha the Great and a holder of vast amounts of land, instructed in her will that upon her death the proceeds from her estate be used to establish the Kamehameha Schools (31) to educate Hawaiians and part Hawaiians to be "industrious men and women." In my opinion, this single act of kindness helped save the Hawaiian race and make it the prominent race that it is today.

The Kamehameha Schools were opened in 1887, and it was the dream of many Hawaiians to attend the school. The school was on the island of Oahu, and students from the neighboring islands boarded on campus and generally had a chance to start in their seventh or ninth grade. I applied but was not accepted for the seventh grade, although it was not much of a surprise because my grades were mediocre. Thus, I had two years to position myself for potential acceptance into Kamehameha Schools. I buckled down during my seventh and eighth grade years at Halaula. I clearly remember asking my mom to wake me up early in the mornings to study and prepare for tests while she went about doing laundry and ironing clothes. Indeed, all this work paid off, as I was accepted for my ninth grade year. Off I went to the Kamehameha Schools in the big city of Honolulu, and for the first time I wore shoes to school. Acceptance to Kamehameha Schools was not dependent on financial status. Room and board and tuition amounted to $100 per year during 1957–61. Amazing.

My academic performance at Kamehameha Schools was a little above average and by my senior year I was in college preparatory classes. However, my stuttering problem continued to plague me, and I was one of a handful of students who were required to attend remedial speech class. Instead of trying to overcome this problem, I took the status quo mode by not asking questions and not volunteering answers in class even though I knew the answer. Was that a good way to approach my problem? No.

After graduation in 1961, I was accepted into the University of Hawaii at Manoa and studied agricultural engineering in a Hawaiian Sugar Planters Association program that was designed to train us to supervise workers on the sugar plantations. However, the program was discontinued during my sophomore year and I switched to horticulture, with no good reason other than the fact that all my previous course credits would count toward a timely graduation. Furthermore, my stuttering problem still plagued me, and I was highly encouraged to seek remedial help but I elected to not try to improve. Instead, I thought of ways to not speak in classes or public. For example, we agriculture students had to take a speech class in which we were required to give persuasive, extemporaneous, and demonstrative speeches. For my demonstrative speech, I got up before the class with my guitar, said "This is how to play Hawaiian slack key guitar," and proceeded to play a slack key song, after which I went back to my seat and that was it!!! The teacher kept waiting for me to say something but that was it from me. I would do almost anything to get out of speaking in public. In June of 1965, I graduated from the University of Hawaii.

MY FIRST JOB: A CALLING TO BE A PLANT PATHOLOGIST

My first priority as I approached graduation was to get a job, especially since I was getting married to my college sweetheart, Carol Viola Kaiawe. A few months before graduating, I saw a job announcement for an Assistant in Plant Pathology (technician) position at the University of Hawaii experiment station on the island of Kauai. I applied and was interviewed by Dr. Eduardo Trujillo, a plant pathologist, who had recently transferred from the Kauai station to the main campus on Oahu. He told me you have bunch of "Cs" but at least you got an "A" in calculus. I was hired, and Dr. Trujillo trained me at the Manoa campus for a couple of months, and off I went with my wife to the Kauai station where I was to carry out technical work for Dr. Trujillo, who remained at the main campus and would supervise me long distance and by periodically coming to Kauai. In other words, I was largely on my own. It turned out to be great.

The first instructions from Dr. Trujillo were to read up on statistics and experimental design, and to work on investigating the cause of a papaya disease that he had observed on Kauai. He told me he was quite sure it was a virus disease and judging by the symptoms it might be tomato spotted wilt, although it had not been previously reported on papaya. With those instructions I set out to determine the cause of this new disease. I looked up some information on tomato spotted wilt virus, grew indicator plants, and did my first inoculation experiments to indicator plants. Local lesions developed on tobacco, *Nicotiana glutinosa*, and on petunia, which was the indicator plant for tomato spotted wilt virus. The lesions that developed looked like those caused by tomato spotted wilt virus in Smith's book on plant virus diseases (49). I was amazed and from that moment I knew that I wanted to be a plant pathologist and investigate plant viruses. I was hooked and absolutely knew I had found my calling, all because someone told me to determine what caused this papaya disease.

As I did more experiments on papaya and other crops, I realized that I needed to learn more about plant pathology and science in order to pursue my calling. I gathered the courage to ask Dr. Trujillo if he would consider accepting me as his student for a Master's degree in Plant Pathology. He said it would be difficult for me to get into graduate school because of my mediocre grades, even though I had performed well as a technician. I do not know what Dr. Trujillo did, but I was accepted as an MS student under Dr. Trujillo in the fall of 1966. Like most things, once you know what you want to do, working hard to be good at it is natural and along with that comes good grades, etc. My master's thesis was on tomato spotted wilt on papaya (29) and on selected lines of tomato and its relatives.

WORDS THAT DEFINED MY APPROACH TO PLANT PATHOLOGY

Eduardo Trujillo is a plant pathologist extraordinaire who is broadly trained in botany and plant pathology. Try as I may, I have never been able to diagnose disease problems as well as he did. Importantly, he instilled in me part of my philosophical approach to plant pathology. As I learned more biochemistry and chemistry, I would discuss and sometimes argue with him over these subjects. But he would tell me: "Dennis, don't just be a test tube scientist, do something to help people."

I completed my MS degree in 1968 and left Hawaii with my wife and two small children, Jennifer and Andrew, to pursue my Ph.D. at the University of California at Davis (UC Davis). UC Davis was an excellent place for my family; it had affordable married student apartments for graduate students who were mainly poor but had hope that a better life was ahead. Our plant pathology department had upward of 40 graduate students, many of whom would become stellar plant pathologists. I was fortunate to meet Dr. Robert Shepherd early on, and I did my dissertation on pea enation mosaic virus under his guidance (27).

Like the rest of the graduate students, I worked hard at my academic classes and my dissertation research. Through his laboratory prowess and his words, Dr. Shepherd taught me my other philosophical approach to plant pathology. A typical research meeting with Shepherd would be as follows: I would eagerly tell him of my experiments and the exciting results. After some discussions he would invariably say, "Now tell me, what have you really accomplished?" It took me a while to get it, but essentially he was saying OK, you have done all these experiments, but what have you accomplished? Did you make meaningful progress toward your objectives? These words forced me to critically separate the chaff from the wheat. The philosophy that I learned from the words of Dr. Trujillo and Dr. Shepherd, "Dennis, don't be just a test tube scientist, do something to help people" and "Now tell me, what have you really accomplished," would guide me through the rest of my career.

THE MOMENT OF TRUTH: OVERCOMING MY STUTTERING PROBLEM

I was doing well on the research and academic side at UC Davis, but my stuttering problem still plagued me. Oral communication was a major deficiency in my repertoire. In my advanced plant pathology class I gave poor oral summations of research papers because of my stuttering habit. At one point, the instructor told me, "You can do good research, but how will you effectively communicate at talks at national meetings?" I was concerned but did not seriously focus on improving. On the bright side, however, I gained much confidence that I really knew my stuff in science and plant pathology.

Four or five months before my projected time to complete my Ph.D., I was invited to interview for an assistant professor position in the plant pathology department at the University of Florida's citrus experiment station in Lake Alfred, Florida. Would I be able to effectively communicate my research results to convince the University of Florida to offer me the job? I prepared thoroughly for the seminar and received coaching and encouragement from Dr. Shepherd and my fellow graduate students. I continually told myself to make the seminar clear and point out how my work had advanced the narrow field of multicomponent viruses. In my bedroom, I practiced and practiced in front of the mirror and pointed to imaginary data slides. I did not rely on note cards because I practiced until the seminar was second nature to me. I was fully prepared, but would my stuttering problem prevent me from communicating effectively? The moment of truth had indeed come.

I flew to Florida and after various activities presented my seminar to a rather large group of scientists and technicians. Incredible as it seems I gave the best talk of my life and did not stutter for a single moment! I have not stuttered since. Hard to believe, but it is true. A miracle? I don't know. The director called me a few days later; he offered me the job and I started in February of 1972. I had killed two birds with one stone: secured a plant pathologist position and licked my psychological problem of stuttering. What ended my stuttering? I believe the confidence that I had gained in myself through the accumulation of knowledge and experimentation and the realization that I was about as good as any of my fellow students played major roles in overcoming my psychological stuttering problem. Naturally, the thorough preparation for the seminar was a key to my performance.

UNIVERSITY OF FLORIDA

My First Collaborator in Science: Let's Go for the Big Enchilada

My primary research responsibility at the University of Florida was to work on young tree decline, a condition that was causing serious problems on citrus trees that were grafted to the industry's dominant rootstock, rough lemon. The cause was not known, and symptoms did not appear in trees less than five years old. However, tenure decisions at the University of Florida were decided in five years. My director Dr. Herman Reitz told me "Dennis, I need something in my hands that

I can show people in Gainesville that you are worthy of tenure." What am I saying here? Working only on young tree decline would have been academic suicide for obtaining tenure; I had to do other things to pass the tenure hurdle. I decided to not even make things close.

Early on, Dr. Steve Garnsey, a plant pathologist at USDA/ARS (United States Department of Agriculture/Agricultural Research Service) in Orlando, and I struck up a friendship and collaboration that would last for life. That collaboration advanced my young career immeasurably. Steve was publishing on the mechanical transmission and preliminary characterization of citrus leaf rugose and citrus variegation viruses. He graciously allowed me to collaborate with him and lead with the more complete characterization of these viruses. We hit a gold mine when we showed that infectivity of nucleic acid component mixtures of these multicomponent viruses could be activated by adding a coat protein of the virus to the nucleic acid mixture. This protein activation phenomenon had been recently reported with alfalfa mosaic virus (3), and it was indeed a hot virology topic. We exploited this advantage and produced a number of good publications (23) while my experiments on young tree decline were still incubating. These studies helped me make it not even close when it came for my tenure and promotion.

Steve and I further collaborated on citrus tristeza virus (CTV), arguably the most important virus disease of citrus worldwide (5). CTV was diagnosed by graft inoculating the Mexican lime indicator plant, which showed vein flecking in 3–18 weeks. Serological tests could not be used for diagnosis because good antiserum to CTV had not been produced. We went for the big enchilada by setting the goal of developing a rapid serological test for detecting CTV. Purification of the CTV had been recently reported but yields were very low. We did initial electron microscopy work and found that young leaves and shoots, and especially the bark tissue, had the highest amount of virus particles. In our collaboration, Garnsey's responsibility was to raise plants and continually supply me young leaves and shoots infected with CTV, while mine was to develop a routine purification system and purify enough virus for fellow collaborator Dan Purcifull at Gainesville to produce antiserum to CTV in rabbits. I recall it took many tissue transfer runs between Orlando and Lake Alfred and purification runs at Lake Alfred before we obtained sufficient amounts of virus for antiserum production. This work paid off handsomely. The CTV antiserum worked very well for diagnosing CTV in infected trees (1, 15, 26). The antiserum was especially valuable in Israel and California, where they were trying to control the spread of CTV by timely detection and tree removal. I regard this as my best work at the University of Florida, as it was true to the philosophical approach to plant pathology that I learned from Drs. Trujillo and Shepherd.

LEAVING THE UNIVERSITY OF FLORIDA: WHAT MAKES A PERSON CHANGE WORK PLACES?

I had just received my tenure and promotion and seemingly was performing at the top of my game in my young career. I don't know for sure why I left the University of Florida, but I had been asking myself in the quiet of my office: "Do I want to be in this position 10 years from now?" I think the most important reason for leaving was that I wanted to broaden my research to a range of crops. The day after the Thanksgiving holiday in 1977, my family and I drove from Florida to the Geneva Campus of Cornell University, where I took a position as a plant pathologist to work on viral diseases.

CORNELL UNIVERSITY: A MAGICAL 25 YEARS OF FUN AND RESEARCH

Our department had a dynamic group of young and energetic scientists that were led by Jim Hunter. We were ambitious and wanted to be outstanding scientists, and got along well and helped each other. I also had the privilege to collaborate with the older but dynamic Dr. Rosario Provvidenti, a vegetable virologist who did great work on identifying sources of resistance to viruses of vegetables (45). My position description was to work on plant viruses that affected economically important crops. Indeed, it was a great place to work.

Synopsis of My Research Efforts

My research encompassed the broad areas of classical and molecular virology. These included development of rapid serological detection of viruses infecting a range of plants, including woody plants (62), vegetables (51), and others such as cardamom (28); development of pseudorecombinants of multicomponent viruses (6, 32); and cross-protection studies on zucchini yellow mosaic (55), tomato ringspot (2), and tomato spotted wilt (57) viruses. Later work led to development and testing of virus-resistant transgenic vegetables (12–14, 22, 58); some work on the mechanism of transgenic virus resistance (40–42); sequencing of viral genomes (33, 38, 63); and risk assessment studies of virus-resistant transgenic plants (11). I also did a lot of international work on a range of viruses, which helped to attract numerous graduate students, postdoctoral associates, and scientists to my laboratory. I carried out a virus-indexing program that was certified by the USDA for the introduction of grapevines to the United States. Grape growers used this program to introduce new cultivars. In my first year at Cornell, I established a papaya ringspot virus (PRSV) research program, which I will describe in more detail below.

Music: The Art of Kanikapila

The above works were done by Ph.D. graduate students, postdoctoral associates, visiting scientists, and excellent technicians. We worked hard but also held fun parties with much food and music. Early on I learned that people enjoy music more if they participate. The Hawaiian term for a sing-along is kanikapila. A successful kanikapila is one where nearly everyone heartily participates, and accomplishing that is the responsibility of the leader. It really is an art. My lab had people from different countries and of different ages, and it was a challenge to include everyone. As we had more kanikapila sessions, the participation became more inclusive and the fun increased. Sometimes we sang into the wee hours of the night. We ended our nights with My Way, our theme song. I maintain that music is the international language and does more to break down barriers than most anything else.

THE PAPAYA STORY: PUTTING IT TOGETHER OVER 34 YEARS

In my "papaya story," I focus more on why we did what we did rather than just review (19) what we did. I hope it illustrates my basic philosophical approaches to plant pathology: "Dennis, don't just be a test tube scientist, do something to help people" and "Now tell me, what have you really accomplished?"

The Beginning: Benefits of Proactive Research

During a vacation in Hawaii in 1978, I was introduced to the Dean of the College of Tropical Agriculture at the University of Hawaii, who asked me, "Dennis, the papaya ringspot virus is in Hilo; what would happen if it got into Puna (19 miles away), where nearly all of Hawaii's papaya is being grown?" Naturally, I said the industry would be devastated. Shortly thereafter, I got modest funding from the dean and started my research on PRSV. My original team included the late University of Hawaii scientist Ryoji Namba (entomologist), Mamoru Ishii (plant pathologist), and my graduate-student-to-be Shyi-Dong Yeh. Our first efforts were simply to purify the virus, produce antiserum, and adapt the ELISA (enzyme-linked immunosorbent assay) test for rapid detection of virus (25). Shyi-Dong Yeh did his Ph.D. research on cross protection to control PRSV. What is the main point here? We started efforts to control PRSV even before it was a serious problem in Hawaii. This timely effort would prove decisive. Research takes time no matter how good or lucky you are.

Cross Protection: Importance of Knowing When to Change a Research Strategy

Cross protection is the phenomenon whereby plants that are systemically infected with a mild strain of a virus become protected against the effects of infection by a more virulent strain. We developed a mild strain of PRSV, designated PRSV HA 5-1, by nitrous acid mutation, and greenhouse trials showed it protected well against the severe Hawaiian strain PRSV HA (60). Starting in 1984, cross protection was deployed in Hawaii and extensively used in Taiwan. The protection results looked promising in Hawaii (8, 37, 43), but the mild strain showed prominent symptoms in the winter months to the point that farmers did not use it extensively. Taiwan deployed cross protection widely at first, but the lack of durable protection did not provide sufficient economic benefit to justify long-term use by growers (56, 59, 61). Extensive tests were done in villages in northeast Thailand but the severe strains overcame the cross-protected plants. Our later experiments showed that cross protection was rather strain-specific (52). I asked myself the question, "Now tell me, what have you really accomplished?" My conclusion was that the approach was not good enough for sustainable control in Hawaii, and I elected to change control strategies. Giving up your favorite toy is not easy, but sometimes you need to do it to make progress.

Retooling My Career: Getting Out of the Comfort Zone

Changing gears in mid-career is not easy. I was trained in the virology of the 1960s, but by the 1980s, it was clear that molecular biology was the rage, and advances in gene cloning and transformation began to make these tools relevant for approaching practical problems in plant pathology. I remember going to meetings, seminars, etc., and listening to molecular biologists expound on research using their jargon, which I could barely understand. Thus, I decided to get out of my comfort zone by at first learning the language of molecular biology, and then I hired a postdoctoral associate to clone the coat protein gene of PRSV and to introduce my lab to the era of molecular biology. Especially in the early stages of retooling, I encouraged my lab people by saying, "Don't worry, once we learn the techniques of molecular biology, we are going to be hard to beat because we are biologists and we know what to do with those techniques." I also took a sabbatical leave to learn the practical aspects of gene cloning.

But first our department at Geneva also had to retool a laboratory for the modern technology. Our then department chair Herb Aldwinckle enthusiastically helped to convert a small seed lab in the basement of Barton Hall into a molecular biology lab. In the next 20 years I dare say that per square foot, that crowded lab, which was used by those who wanted to do molecular work, was one of the most productive spaces at Cornell University.

The classic papers by Roger Beachy and colleagues (44), which showed that transgenic tobacco and tomato expressing the coat protein gene of tobacco mosaic were resistant to this virus, and Sanford & Johnston (47), which focused on the concept of parasite-derived resistance, were published in 1985–86 and gave myself and many other plant pathologists the experimental and conceptual breakthroughs that provided a clear path to virus control through the development of virus-resistant transgenic plants. The second phase of the papaya story had begun.

The Transgenic Papaya Research Team: A Blend of Expertise with a Focused Mission

The assemblage of the transgenic papaya team started around 1985 when Dr. Jerry Slightom, an excellent molecular biologist at Upjohn Company, which had recently acquired Asgrow Seed Company, contacted me about developing transgenic vegetables for resistance to the important viruses of vegetables. I told him the important viruses were zucchini yellow mosaic, watermelon mosaic virus 2, papaya ringspot, and cucumber mosaic viruses and also informed him that we had cloned the PRSV HA 5-1 coat protein gene. Naturally, we had mutual interests in PRSV for resistance in cucurbits and papaya. Shortly thereafter Dr. Richard Manshardt, a horticulturist at the University of Hawaii, and Maureen Fitch, a graduate student of Manshardt and also an employee of USDA/ARS in Hawaii, joined the team. Steve Ferreira of the University of Hawaii joined the team a few years later. This team had an excellent blend of expertise and was focused on controlling PRSV in papaya using the pathogen-derived resistance approach. This highly focused research helped us stay the course and avoid temptations to pursue more noteworthy academic directions.

Papaya Ringspot Virus–Resistant Transgenic Papaya Is Developed: Going for the Jugular

The details of the development of the transgenic papaya have been reviewed extensively (19), so I simply summarize research from 1985–1991 in this paragraph. After we cloned the coat protein gene of PRSV HA 5-1, Jerry Slightom sequenced it and engineered it into a binary vector. Maureen Fitch had prepared zygotic embryos at the University of Hawaii, and she and Richard Manshardt came to Cornell's Geneva campus, where we used the gene gun to bombard the embryos with tungsten beads coated with DNA that contained the coat protein gene and necessary regulatory and selection elements. This was done under the watchful eyes and good suggestions of John Sanford, the coinventor of the gene gun. Maureen and Richard took the bombarded calli back to Hawaii, regenerated transgenic lines, made cloned tissue culture plantlets of several transgenic lines, and sent the lines to me for inoculation by PRSV HA under greenhouse conditions. Cloned R0 plants of line 55-1 showed resistance (10); this was in early 1991, six years after cloning the gene of PRSV. Yes, research takes time.

After the R0 plants showed resistance to PRSV HA in the greenhouse, we elected to make cloned plants of the R0-resistant line and test them for resistance under field conditions. The conventional route would have been to produce R1 and R2 plants, do more greenhouse inoculations, and then select the best progenies for field trials, a process of 2–3 years. My philosophy was that determining resistance under field conditions was the most important criteria, and it was best to find out as soon as possible. In other words, go for the jugular. In April 2002, Richard Manshardt started a field trial of R0 plants of line 55-1 at the University of Hawaii experiment station on Oahu Island. That decision would have profound implications.

Papaya Ringspot Virus Invades Puna and Rainbow Is Developed: Performing Under Pressure

In early May 1992, Steve Ferreira and I landed at the Honolulu airport after a trip to Guam and were asked to immediately fly to Hawaii Island. The long-awaited invasion of PRSV had begun in Puna, where 95% of Hawaii's papaya was produced. The Hawaii Department of Agriculture's efforts to contain the virus by rouging did not stem its spread, and this effort was abandoned in

1994, allowing PRSV to spread even faster. By 1998, papaya production in Puna was reduced to 26 million pounds compared with 52 million pounds in 1992 (18, 20). It was difficult to find healthy papaya trees. The industry was in a crisis.

Ironically, by December 1992 results from the Oahu field trial showed that R0 plants of line 55-1 were resistant to PRSV (34). A potential solution was in sight. Richard Manshardt used plants from the R0 field trial to develop the SunUp and Rainbow cultivars in the ensuing three years. Briefly, we had transformed the commercial red-fleshed Sunset cultivar from which we obtained line 55-1. SunUp (36) is line 55-1 made homozygous for the coat protein gene, and Rainbow (36) is an R1 hybrid of a cross between SunUp and the nontransgenic Kapoho papaya, the then-dominant cultivar in Puna. In 1995, Steve Ferreira started a large field trial of SunUp and Rainbow in a Puna farm that was devastated by PRSV. This key field trial (9) convinced scientists, growers, and packers that Rainbow and SunUp were indeed resistant under Puna conditions and had excellent horticultural properties. There was hope.

However, tensions were very high and a number of growers felt our work would not succeed. For example, in 1995, at a grower meeting with video cameras running, a papaya farmer said that the transgenic papaya would not work, and even if it worked we would not be able to get the licenses for commercialization because the big companies had intellectual rights to some of the technologies and would charge millions of dollars for the license, and also remarked that we were ivory tower scientists. I was upset at those statements and when I gave my talk I told them that indeed everyone would be able to see whether the transgenic papaya would be resistant because Steve Ferreira had started a field trial in Puna. As noted above, the results from the field trial were beautiful, and the consensus was that we had an excellent transgenic papaya that was resistant to PRSV (9). In retrospect, however, the behavior of the few farmers was understandable because they were seeing their papaya crops melt under the attack of PRSV. When they finally saw the fruit and plants in the field trial, they were happy, but we told them they could not have it just yet because it still needed to be deregulated. What an exciting life, even when performing under pressure.

Deregulation and Commercialization of the Transgenic Papaya: The Red Zone

"The team has entered the red zone. Let's see if they can score a touchdown." American football broadcasters often say this or something similar to emphasize that it is great to move the football down the field but the obvious goal is to score. The team that consistently scores touchdowns when in the red zone, which is from 20 yards onward to the goal, usually wins the game.

What we had done through the field trial would only be academic unless the papaya got through the red zone of translational biotechnology, which I regarded as getting the papaya deregulated and commercialized. The papaya industry had no expertise or finances to do this work. So the team entered the red zone. We did the necessary experiments, compiled data, and filled out the applications with limited financial support that was largely provided by earmarks obtained by Hawaii's congressional delegation. The first petition was filed at the end of 1995 and by the end of 1997, we had cleared the USDA Animal Plant Health Inspection Services (APHIS) for environmental safety and the Environmental Protection Agency (EPA) for tolerance levels of coat protein because it regarded the coat protein as a pesticide, and completed consultation with Food and Drug Administration (FDA) for food safety (19). The Papaya Administration Committee (PAC), a USDA marketing order consisting of Hawaii papaya growers, obtained the necessary licenses to commercialize the transgenic papaya (19). On May 1, 1998, the PAC held a celebration in Hilo and distributed the seeds free to growers on a lottery system based on the amount of damage the growers had experienced (16, 17). The celebration was held 20 years after I had started research on PRSV and six years after the invasion of PRSV into Puna.

What did I learn from this? One has to be the eternal optimist and not let perceptions stop you from doing things that are out of your comfort zone. And the philosophies learned early on: "Dennis, don't just be a test tube scientist, do something to help people" and "Now tell me, what have you really accomplished?" rang especially true in the red zone of translational biotechnology.

The Transgenic Papaya Then and Now: Somewhere Over the Rainbow, Dreams Really Do Come True

From the start, the growers preferred the yellow flesh Rainbow transgenic papaya. During the first two years of release (1998–1999), my wife Carol did a master's research thesis on the adoption of the transgenic papaya. Her results documented the rapid adoption by farmers, with the primary reason for adoption being the resistance to PRSV (16, 17). A snapshot survey taken in 2011 again showed that farmers select the transgenic papaya because of its resistance to PRSV (18).

The PRSV resistance of the transgenic papaya has remained durable, and consumers have readily accepted it. Today, the transgenic papaya makes up approximately 85% of the Hawaiian papaya crop (21). I think it is safe to say that the transgenic papaya saved Hawaii's papaya industry. Furthermore, it was the first public-sector-developed transgenic crop to be deregulated and commercialized in the United States. One might say it was a poor man's transgenic project.

USDA PACIFIC BASIN AGRICULTURAL RESEARCH CENTER IN HAWAII: AN ADVENTURE IN LEADERSHIP

I retired from Cornell University in May 2002 and became the director of the USDA Pacific Basin Agricultural Research Center (PBARC) in Hilo, Hawaii. Why did I leave such a great position at Cornell University that I enjoyed so much? I guess I felt that it was time to repay Hawaii for all the good things it had done for me. When the USDA interviewers asked me why I would leave Cornell for PBARC I answered, "I was born and raised on a sugar plantation in Hawaii, so I know what it is to live in Hawaii, and I spent 34 years away on the mainland United States and competed successfully at a high level. I am confident that I can make PBARC a great research center, but do it local style, if you know what I mean." I wanted PBARC to really help its clientele in Hawaii and the Pacific. In my mind, I wanted to make PBARC shine like the experiment station at Cornell's Geneva campus. In May 2002, I left behind the most enjoyable 25 years of my research life.

My responsibilities at PBARC were to direct the center, to lead the building of a new physical facility, and to carry on an active research program. I realized I could not do a good job with the first two responsibilities and still carry on a large research program. However, my goal was to do research that would have significant impact.

Ten Years at PBARC: Now Tell Me, What Have You Really Accomplished?

We completed three phases of the four planned phases of PBARC: half the laboratory research building, a large addition to the building to house technical workers and visiting scientists and a conference/seminar room, and a headhouse/greenhouse complex. We had obtained nearly all funds for the fourth phase, which was the other half of the laboratory research building, but, unfortunately, congressional cut backs forced the rescinding of the earmark funds for this final phase.

My approach as director was to exert leadership in direction, to cheer on colleagues, to seek more funding for the center, and to make the center more relevant to agriculture in Hawaii and other tropical regions of the Pacific. By the time I completed my stint, Hawaii stakeholders were well aware of what we did. We had done much work for Hawaii, and our clientele were fully supportive of PBARC. I would like to single out, particularly, the area-wide fruit fly control program (54) funded by the USDA. The program had started a year before I came to PBARC, and it became one of the darlings of ARS, directly benefitting Hawaii growers and homeowners and also garnering a number of prestigious USDA awards.

The PBARC band was one of my more significant achievements at PBARC. To loosen up PBARC, I started a band that would sing and provide music at holiday parties. Practice was very informal and done usually during the lunch break. Then we went public with a hula troupe of ladies from PBARC that danced at the dedications of the different PBARC building phases. The band and the hula troupe brought many people together; we had fun, and we let the public know that we did good research and had a good time.

My research efforts continued on papaya, mainly focusing on transgene flow from Rainbow to neighboring nontransgenic fields (24) and detailed characterization of the transgenic papaya during our efforts to successfully deregulate the transgenic papaya in Japan (7, 50, 53). Arguably, the Hawaiian transgenic papaya is one of the most well-characterized commercial transgenic crops. A draft genome of the transgenic papaya has been published (39).

Canada deregulated our transgenic papaya rather quickly, as they accepted the work done by the US agencies (APHIS, EPA, and FDA). Hawaii started exporting transgenic papaya to Canada in 2003 (21). Today, it is a significant market for Hawaii's transgenic papaya.

It took us more than a decade to deregulate the transgenic papaya in Japan. The papaya industry again asked the original papaya team for help to deregulate the transgenic papaya in Japan. We started in 1999, picked up momentum in 2002 when I moved to PBARC, and finally got it deregulated in December 2011 (21). This effort taught me the value of tenacity and perseverance. Many people said we would not succeed. In fact, some of my friends would periodically ask me how things were coming with the Japan project; I would say fine and that we were getting closer, and they would jokingly say "Dennis, you told me that last year!" But in the end, I had the last laugh.

In September 2011, Carol and I were invited by the USDA Foreign Agriculture Service to a Biotechnology Conference in Japan to advertise the impending release of the transgenic papaya in December. I gave a talk on the transgenic papaya and helped kicked off a Hawaiian Luau at the US Embassy. During the last part of my talk, while I flashed pictures of the many people that helped in the papaya project, Carol and I sang "Somewhere Over the Rainbow/What a Wonderful World," which had been made famous by the late Israel Kamakawiwo'ole. Music indeed is the international language.

As a last research act, in October 2012 I submitted a petition to deregulate the transgenic papaya in China. Scientists at PBARC (now called the Daniel K. Inouye US PBARC) and at the University of Hawaii at Manoa are moving this effort forward.

THE HUMAN SIDE OF BIOTECHNOLOGY

As I get ready to sum up this chapter, I must briefly describe my Thailand experience to emphasize that we need to keep in mind the human side of biotechnology.

In 1987, I was part of a USAID (United States Agency for International Development) project that was aimed at helping farmers in northeast Thailand. My focus was on controlling PRSV in the backyards of households where papaya was commonly grown for green papaya salad called somptum. This effort was led by Vilai Prasartsee of Thailand's Department of Agriculture (DOA); a dedicated scientist that knew all aspects of papaya culture in the villages. We tried mild-strain cross protection with our PRSV HA 5-1, but the Thai PRSV strains overcame the resistance. I

Figure 1

Thai lady planting cross-protected papaya seedling near her home in a village in Northeast Thailand, 1987.

introduced a PRSV-tolerant papaya cultivar that had been developed in Florida, and Vilai deftly used this germplasm to develop cultivars that became infected by PRSV but showed sufficient tolerance to allow harvest of fruit (30).

In 1994, Thailand's DOA asked my laboratory to help them develop transgenic papaya using the coat protein gene of PRSV from Thailand. The plan was that they would provide nominal funding for supplies and send a scientist to my lab to receive training and do the work to produce a virus-resistant transgenic papaya from the large-fruited Thai cultivars Kaekdum and Kaeknuan. By 1996, some lines showed resistance to PRSV in the greenhouse at Cornell, and in 1997 Carol and I took the lines and tissue-cultured plants to Thailand, as the Thai scientist had left the laboratory a few months earlier. In the ensuing six years, the Thai scientists of DOA selected several PRSV-resistant lines with good horticultural characteristics. By 2004, the group had done a range of risk assessment and rabbit feeding studies that were aimed at providing the necessary information to deregulate the transgenic papaya (46). We were full of hope.

On July 27, 2004, Greenpeace traversed the fence surrounding the transgenic trials, threw fruit in barrels and displayed a large sign "Stop GMO field trials, Greenpeace." The controversy ballooned nationally, and the project was essentially killed. The episode was chronicled by Davidson in 2008 (4) and very recently by Lynas & Evanega (formerly Davidson) (35). This is one of the most disappointing failures of my life.

In nearly every talk that I now give on the transgenic papaya, I end up showing a picture that I took in 1987 of my late Thai lady friend (**Figure 1**). The picture shows her planting a cross-protected papaya seedling that did not resist the virus and reminds me of my dream that did not come true: to deliver a PRSV-resistant transgenic papaya to her home. I do not have the answers to today's GMO controversies, but I am convinced that if we focus on the human side of biotechnology, we can navigate the red zone of the controversy.

THE WAYWARD HAWAIIAN BOY RETURNS HOME

I retired at the end of 2012 from PBARC, which is located only 80 miles from the now abandoned plantation camp where I was born and raised. I still visit with some of my childhood friends from the sugar plantation camp days. As I look back, plant pathology provided me a great career because a person named Dr. Eduardo Trujillo gave this wayward Hawaiian boy a chance.

To those of you starting out in plant pathology, I wish you great experiences. If I may, I would like to repeat the words that were spoken to me many years ago: "Dennis, don't just be a test tube scientist, do something to help people" and "Now tell me, what have you really accomplished?" And allow me to add some of my own words, "Keep in mind the human side of plant pathology."

Aloha.

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