ASPB Pioneer Member

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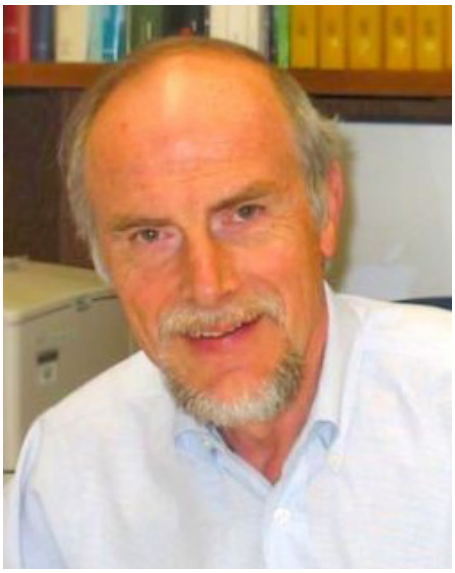

I am a big-city boy, a rarity in the field of maize genetics, where I started working over 50 years ago. I was born and grew up in downtown Santiago, the capital of Chile, and was fortunate to attend a school that both offered a strong all-around curriculum and emphasized English as a second language. In our school system at the time, we took Biology, Chemistry and Physics courses each of our last three years of high school. Biology was one of my favorite subjects, but I was not too keen on its more descriptive aspects, so when I learned about the precision of Mendelian inheritance in my senior year course, I became fascinated with genetics and thought that I might want to study it someday.

As the beneficiary of an academic scholarship from the University of Notre Dame, I came to the US to pursue a college education and ended up staying for life. The two genetics courses I took from Harvey Bender at Notre Dame only confirmed my earlier interests and motivated me to pursue graduate work in genetics. Harvey suggested I apply to several grad schools but living on the tight budget of an academic scholarship with income from summertime jobs, I only applied to five. One of them was the Genetics Department at the University of Wisconsin, where I was lucky enough to be offered a Research Assistantship by Jerry Kermicle. Working in Jerry's lab was a great introduction to the complexity of maize genetics. At the time, students in his lab were working on projects as varied as paramutation, transposition, compound alleles, and nondisjunction. My Ph.D. thesis dealt primarily with the genetic structure of the *R:r* complex allele, the project assigned to me by Jerry, but it also included a chapter on *Lc*, a leaf color marker used in recombination studies; I found it to be a displaced duplication of the *R* locus, raising questions about its validity as a genetic marker. I remember the thrill of that discovery. While minor, it made me confident that, as a graduate student, I too could find new things! The formal genetics training I gained in Jerry's lab, for which I will be always grateful, served me well throughout my career.

Though my Ph.D. minor was in Biochemistry, I realized I needed some hands-on biochemical research experience and sought the advice of Oliver Nelson, another maize geneticist who had joined the department a few years earlier. Much to my surprise and excitement, he offered me a postdoctoral position in his lab, which I very gladly accepted. So, from Jerry's lab on the second floor of the Genetics building, I moved to Oliver's lab in the basement, a truly short trip to start a postdoc. There, Curt Hannah was finishing his Ph.D. on the genetic control of ADPG pyrophosphorylase, the key enzyme in starch biosynthesis. As members of the same departmental poker group, Curt and I knew each other well and he graciously agreed to walk me through the initial techniques in enzymology and protein purification that I needed to get my research going. In Oliver's lab, I began working on the *bronze* (*bz*) locus, and actually I have never stopped. My main postdoctoral project with Oliver was to figure out the effect of *Ds* transposable elements described by Barbara McClintock's on expression of the UFGT flavonoid biosynthetic enzyme encoded by the *bz* locus. So, I acquired and read all the Carnegie Institute Yearbook publications that Barbara had published annually for close to three decades. Fortunately, Oliver sent me to discuss my research with Barbara at the Cold Spring Harbor Laboratory in Long Island, NY, which ended up being as fantastic an experience for me as it would have been for anybody interested in biology and, particularly, in transposons. Besides discussing research with her for

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the better part of an afternoon and evening, I ended up eating breakfast with her the following morning. Because the limo to the airport came to pick me up before the Lab's cafeteria opened, Barbara insisted on cooking breakfast for the two of us in her lab. Not too many people can claim that they were asked by Barbara McClintock: "how would you like your egg?"

My postdoc in the Nelson lab resulted in the publication of several papers, including a couple in the *Proceedings of the National Academy of Sciences* (*PNAS*), which landed me a job in the Genetics Department at Iowa State University. At Iowa State I continued work on the genetic control of flavonoid biosynthesis that I had initiated in Oliver's lab, and I found that the *c2* locus encoded chalcone synthase (CHS), the key enzyme in the pathway, and that mutations in three other genes, *-r*, *c*, and *vp-*, affected the levels not only of CHS, but also of the *bz*-encoded UFGT, so these genes were likely to be regulatory for the whole pathway, a conjecture validated later by work in other labs.

I stayed at Iowa State for just a couple of years. My career in the academic world was interrupted when, at the 1981 International Botanical Congress in Sidney, John Bedbrook offered me a very attractive position as Director of Plant Genetics in Advanced Genetic Sciences (AGS), an ag biotech company that had recently formed in the San Francisco Bay Area. I accepted this position after discussing it with my wife, who was very eager to leave the cold midwestern winters behind. One of my first hires was Rich Jorgensen, who brought to the lab his *Tn5* bacterial transposon expertise, and introduced me to Southern blots, my first experiments in molecular biology. Rich soon formed his own group and, with his wife Carolyn Napoli, went on to discover the now well-known epigenetic phenomenon of co-suppression while working at AGS.

At AGS I had the privilege to work with several experienced and gifted molecular geneticists -Jonathan Jones, Ed Ralston, Diane Burgess, and George Chuck, among them. During my 12 years there, my lab published several papers, two of which are worthy of mention because of their actual colorfulness. The first one is a 1989 paper in *Science* by Jones *et al*., a collaboration with Pal Maliga, also in AGS at the time, describing a visual assay for transposition of the maize *Ac* element in tobacco seedlings, which enabled us to easily quantify both germinal and somatic transposition frequencies in dicots. And the second one is a 1993 paper in *The Plant Cell* by Chuck *et al.*, describing the first example of heterologous transposon tagging, the cloning of a petunia flower color gene with the maize *Ac* element. The flower phenotype produced by the mutable allele made the journal's cover and is the most beautiful, variegated phenotype I have ever seen.

In 1994, I left AGS, which by then was called DNAP, for a Professorial position at the Waksman Institute in Rutgers University, and I stayed there until my retirement. I am particularly grateful to Pal Maliga and Jo Messing (Jo passed away unexpectedly in 2019) for recruiting me to the Institute and providing the opportunity to return to academia. At Rutgers, I met and worked with many wonderfully talented students, postdocs, and colleagues, some of whose contributions I would like to highlight.

My postdoc, Huihua Fu, was key to much of the lab's subsequent success, because she created the ability to isolate large, specific regions of the genome in bacterial artificial chromosomes (BACs) when that was very difficult to do. Huihua, together with my postdocs Xianghe Yan and Wonkeun Park and my first graduate student Binzhang Shen, sequenced and characterized the *bz* region of the *BzMcC* allele that we had earlier shown to be highly recombinogenic, and established that it occurred in an unusually gene-rich region of the genome. She also cloned the *bz* region of the B73 inbred and reported, in a widely cited 2002 *PNAS* paper, that the two allelic regions were highly polymorphic, only sharing genes and differing in all the intergenic retrotransposons and what appeared to be partial genes. These particular genes were later shown by postdocs Yubin Li and Jinsheng Lai, in collaborative work with the Messing

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lab, to be gene fragments borne on *Helitrons*, a recently discovered class of DNA transposon. Subsequently, my postdoc Qinghua Wang took over this project and showed that every maize inbred line that she looked at was remarkably different, the common features being genes and occasional transposon clusters that revealed a relatively recent common ancestry.

Most of the projects in my lab at Rutgers dealt with a genetic problem, usually involving meiotic recombination or transposition. In general, transposon projects were taken up by my students and postdocs and recombination studies were done by me and my expert lab manager, Limei He, because they took longer, and I could not conscionably assign them to a grad student or postdoc. New, genetically active DNA transposons belonging to most major families were characterized in the lab. Xianghe Yan and my student Zhennan Xu identified *Jittery*, a new autonomous element of the *Mutator* superfamily with homology to a transcription factor and Yubin Li identified *TED*, another autonomous element of the *Mutator* family that is unusual because of its high gametophytic excision frequency. Zhennan also characterized *Mx* and *rMx*, a new pair of autonomous-nonautonomous members of the *hAT* transposon superfamily to which *Ac* and *Ds* belong. Finally, Jun Huang -my last graduate student- showed that *Ac* and *Ds* transposons more than 100 kb apart were capable of transposing, as well as inverting and rearranging the entire DNA fragment between them, providing evidence for the existence of the macrotransposition events that Ed Ralston, Jim English, and I had postulated years earlier. An important issue regarding the retrotransposon and *Helitron* structural polymorphisms we had uncovered around *bz* was whether they affected recombination in adjacent regions, and, with Limei, we were able to take advantage of the high genetic resolution provided by the *bz* genomic region to show that they do.

Yubin Li was also the prime mover of a long-term NSF-funded lab project to create a user-friendly, sequence-indexed reverse genetics resource for maize based on a visually tractable *Ds* element. This element, engineered by my postdoc Gregorio Segal, carries a Green Fluorescent Protein gene that is expressed in the endosperm. In collaboration with our bioinformatician colleagues, Charles Du and Wenwei Xhiong at neighboring Montclair State University, the lab generated over 14,000 sequence-indexed insertions, most of which were deposited in the Maize Genetics Cooperation Stock Center and are listed in the Maize Genetics and Genomics Database. In my last few years at Rutgers, Charles' lab and mine were involved in another collaborative project involving large genetics and genomics datasets, which led to the unexpected finding that select low-copy retrotransposons can be very active in the pollen of some maize inbreds, but not others, and could account for the vast majority of spontaneous mutations in maize.

When I started my graduate work in maize genetics, I did not realize how rare it was then for "city boys" to work with maize until I heard a comment to that effect at one of the earliest Maize Genetics Meetings I attended in Allerton Park, IL. But I fell in love with the field and stayed in it, literally, for over 50 years, managing to grow a maize genetics nursery every one of those years. One summer, I even made pollinations with my entire left leg in a plaster cast, the product of a soccer-incurred fracture! I must add, parenthetically, that this experience did not diminish my passion for either maize genetics or soccer. If I had a word of advice for young people contemplating research careers, it would be simply that, though there may be multiple alternative paths to a productive career, most perhaps unpredictable, you must enjoy doing whatever you choose to do.