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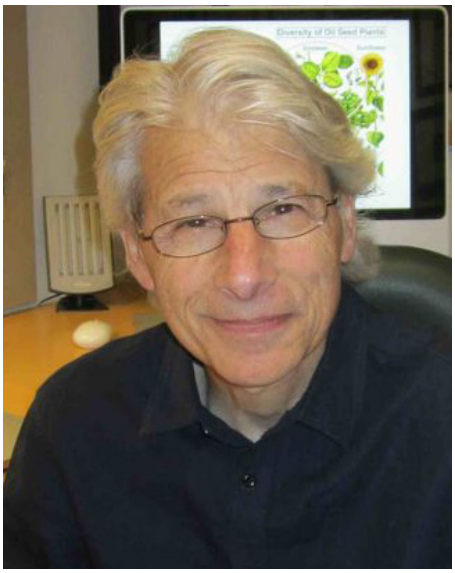
Bob Goldberg



How did you spend your career?

If someone had asked my family or friends back in the 1950s when I was growing up in Cleveland, Ohio if Bob Goldberg was going to be a scientist when he "grew up" they would respond emphatically "are you crazy…there is no way!" School was not something that I was very interested in or that I spent much time working on. I was more interested in baseball, little league, playing pickup in my neighborhood, or going to see the Indians' games with my parents and sisters. In fact, my uncle owned the dry cleaners that cleaned the Indians' uniforms. I spent many a summer day in the clubhouse with future Hall of Famers such as Bob Feller, Early Wynn, Al Rosen, Satchel Paige, and others collecting their dirty uniforms for cleaning. In school, I was bored by the narrow, authoritarian teaching of the day, the rote learning, and teachers that spent more time trying to cram facts and figures down our throats than trying to inspire and connect the subject matter to the problems and realities of life. And, I might add, hitting us with a paddle or a ruler if we disobeyed or challenged the norms and rules of that time. I learned my ABCs as one had to do to get by and graduated from high school in the spring of 1962. I didn't enter any science contests, collect insects, spend time after school marveling at the wonders of chemistry and physics, or win any academic awards for excellence. However, I did have one distinction—the record for the number of detentions after school in the principal's office that still stands to this day! Looking back, my antics in the classroom were driven primarily by boredom and as a protest against the monotonous teaching of the day. Teaching that inspired me indirectly throughout my career to make my classes as exciting, relevant, and inspiring for my students as they could be—a quest that, ironically, has been one of my major passions and successes during my five-decade career as a science professor.

So, how did I wind up becoming a scientist and having a "Cinderella-like" career over the past 50 years? Despite my lack of effort in high school, I knew that I would go to college and, in those days, if you graduated from high school with at least a C average you were automatically admitted to a state college—unlike current admissions policies. I decided to go to Ohio University (OU), a small, bucolic school in the Appalachian foothills of southeastern Ohio and the oldest public university in the United States outside of the original 13 colonies. I had no clue as to what I was going to major in or pursue as a career if I was able to graduate from college, given my very poor high school record. Fall of 1962 was a memorable one in history and for myself. The U.S. confronted the Soviets in the October Cuban Missile Crisis shortly after I arrived at OU. It was a very scary time and we spent lots of time watching the evening news with Walter Cronkite and practicing survival skills in radiation fallout shelters hoping that the world would avoid a nuclear catastrophe, which we did thanks to President Kennedy. Little did we know that he would be killed by an assassin's bullet a year later changing the course of history. Nevertheless, fall classes went on as usual. As a freshman, I enrolled in The University College which was required of all first-year students. It had a standard liberal arts curriculum and allowed new students to adjust to college life and find a subject area they might want to major in starting in their second year. My life was changed forever when I enrolled in an introductory biology class taught by Professor Norman Cohn, a young plant cytologist who had just received his PhD from Professor C.P. Swanson at Johns Hopkins, the preeminent

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plant cytogeneticist of that era. Norm was unlike any teacher I had ever had—dynamic, witty, brilliant, and a "teacher's-teacher." He opened my eyes to the excitement of science and discovery, the importance of biology to our lives, and most importantly, how to think critically. Norm's class focused mostly on cellular and molecular processes, and what we now call molecular biology. Looking back, this was only nine years after the discovery of the DNA double helix and four years before the genetic code was cracked. Although little was understood about molecular processes in living cells, Norm focused on the current state of knowledge and raised questions about the future—what could be known? I recognized immediately that this presented an enormous opportunity and that if one decided to explore the molecular aspects of how genes work the future was wide open. My eyes were opened for the first time about a subject that I could spend a lifetime thinking about if I was dedicated and smart enough to conquer the rigors of science—something that I did not do very well in in my journey leading to college. This was also a time when the U.S. was making a big push in STEM in order to catch up with the Soviets in the "space race." Pursuing science as a career was emphasized and there was a lot of financial support for students such as myself. My hopes were raised when all of my energies studying long hours in the cavern-like Chubb Library during my first college semester came to fruition and I achieved a 3.5 GPA and an A in Norm's biology class. In fact, my high school friends were "shocked" by my academic performance, my parents said that they always knew I "could do it," and I obtained enough confidence in my abilities that I challenged myself to reach for higher heights. Once I decided on a science trajectory, Norm and his wife Peggy—also a scientist and Dean of the Honors College—were my cheerleaders, mentors, and friends for over 40 years until they both passed about a decade ago.

I was caught in a dilemma, however. During that memorable fall semester, I also took classes on U.S. government and history and I was mesmerized by the topics covered, particularly constitutional law. This was at a time when the civil rights movement was just beginning and major Supreme Court decisions were changing our lives for the better (e.g., the right to remain silent). In fact, the "March on Washington" and Martin Luther King's famous "I have a Dream" speech occurred in the Summer of 1963 after my first year at OU. I thought that the possibilities for the future to participate in a "revolution" to make lives of people better were wide open and that it would be exciting to pursue law and, eventually, argue cases before the Supreme Court. I was faced with a Solomon's choice when I returned to OU in the fall of my second year and had to declare a major…science or the law? In the end, I decided to major in botany and take a science path because it was more challenging for me than the law, and provided unlimited opportunity to peel away some of nature's mysteries. Nevertheless, I continued to pursue my interest in the law on the side. As a result, I graduated from OU in 1966 I had taken enough courses to earn a minor in political science.

Why did I decide to study botany and focus on plants? That decision was simple. In that era multidisciplinary biology departments or specialized programs in molecular and cellular biology did not exist. You had a choice of majoring in botany, bacteriology, or zoology…period! The thought of dissecting animals and human corpses in the zoology courses that my pre-med friends were taking didn't appeal to me, nor did studying bacteria. Norm Cohn's lab was in the Botany Department, as were most of the molecular- and genetics-oriented courses. Norm had asked me if I would join his lab as an undergraduate student and study root cytology. It was there that I also crossed paths with Ralph Quatrano who was working on his master's degree in Norm's lab. Ralph was my introductory botany TA. He mentored me about plants in the lab and became a life-long friend and colleague during his decades-long career as a distinguished plant scientist. I was fascinated by plant reproduction and development. I enjoyed my plant ecology, morphology, taxonomy, and physiology classes, as

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well as the genetics courses that were dearer to my heart. I spent many enjoyable weekend days collecting and classifying leaves and twigs for my botany labs from the different trees growing in the woods surrounding Athens. I spent my sophomore and junior years in Norm's lab learning about research and carrying out cytological experiments on root growth. I don't think I was very good at the bench, and four decades later when I was elected to the National Academy of Sciences, Norm sent me my undergraduate root section slides as a gift with a congratulatory note that said, "to my best undergraduate student who never could make publishable slides!" That was Norm's wry humor. In my senior year I had to carry out a year-long undergraduate honors research project. Norm was on sabbatical, so I moved to John McQuate's lab in the Zoology Department. John was my professor in several genetics classes and a classical fly geneticist. I spent long hours in his lab honing my genetics skills, making media, mating flies, and injecting chemicals into their abdomens to determine if the chemicals were mutagens, a subject of intense focus in the 1960s. I wrote an undergraduate honors thesis, "The Mutagenic Effects of Actinomycin D and Mitomycin C on *Drosophila melanogaster*." I presented my research results in my first scientific talk at the annual meeting of the Ohio Academy of Sciences in a large auditorium on the Ohio State University campus, our large sister state college 50 miles to the north. I really enjoyed the process of telling a research story, making projection slides that highlighted my data, and most importantly, speaking in front of a large audience—an endeavor that my speech classes in high school and college prepared me for. By the time I graduated from OU, I knew that I was on the correct path no matter where the journey took me. A life in science was going to be exciting.

My next step was graduate school, pursuing a PhD in genetics. In the 1960s, genetic engineering and the biotechnology industry hadn't been invented yet. If you wanted to pursue a research career in the biological sciences, there was one choice—become a college professor and carry out academic research and teaching. I applied to several genetics graduate programs across the U.S. thinking that my academic record and research experience would carry the day and land me in an excellent program, whatever that was. However, I made a big mistake, a mistake that was the second defining event of my scientific career. I decided to rebel against the Graduate Record Exam (GRE) requirement for admission to PhD programs and randomly marked the GRE in order to get back in the lab as quickly as possible to continue my fly research. Needless to say, I was rejected by almost all of the programs I applied to with an accompanying letter indicating that they were confused why I did so poorly on the GRE Exam and would consider me again if I took the exam over in light of my outstanding academic record. I made the fateful decision to write back and say that I had proved myself in academics and research as an undergraduate and, if they couldn't evaluate me on the basis of my academic record, I was not interested in their PhD program! Ironically, this decision turned out to be one of the best I ever made in my life. What was I going to do now? The Vietnam war was raging and I had to be in school in order to get a deferment from the draft. In addition, I wanted to go to graduate school and continue my science journey. I went back to the Chubb library where the catalogs of all U.S. universities were housed on old, dusty library stacks. I decided to pick one school randomly beginning with the letter A, which turned out to be the University of Arizona (U of A). In those days, U of A was a relatively undistinguished school in Tucson, a small, dusty town in the middle of the Sonoran Desert. Much to my surprise, the U of A had a new interdisciplinary genetics PhD program. One faculty member, Albert Siegel, who became my PhD thesis advisor, received his PhD in genetics from Caltech, under the direction of Max Delbruck (one of the founders of molecular genetics and a future Nobel Laureate). As I discovered, Albert was one of the world leaders in plant virology and was using mutagens to knock-out and identify genes important for

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virus replication. This was precisely my research interest at the time. My thoughts were, I am going to apply to the U of A and if I can't get into their genetics program I am going to Vietnam! At the time I was living in a small trailer in the woods, a short distance from the OU campus. Shortly after I mailed the relevant application material to the U of A with a letter explaining why I did terribly on the GRE, I got a phone call from Bob Harris, head of the U of A Genetics Program, telling me I was admitted to their PhD program and was awarded a five-year National Defense Education Act (NDEA) fellowship. The fellowship paid a $2,100 yearly stipend and all tuition and fees. I was overjoyed at the thought of heading to Tucson, beginning a new life adventure, continuing my research in genetics, and saying good-bye to the frigid Ohio winters. Sunshine here I come!

I barnstormed across the U.S. on my way to Arizona with a couple of friends in my new burgundy Pontiac GTO, much like in the 1960s TV show "Route 66." I fell in love with Tucson and the U of A campus the minute I arrived. The warm, dry desert air, unique forests of Saguaro cactus with large "arms" reaching out as if they were trying to greet you, and beautiful mountains circling the city. A perfect desert postcard and a world completely different from my life in Ohio! The Genetics Program turned out to be better and more intellectually rigorous than anything that I ever imagined. In fact, from the beginning I knew that I had made the perfect choice for graduate school. I relished that I was not at Harvard, or Yale, or one of the other schools that had rejected me. We were a close-knit group of students and faculty with a lot of camaraderie, and knew we were underdogs in the backwater of academia. Collectively, we had the goal of landing on the map someday by caring out excellent research. The Genetics Program emphasized a multidisciplinary approach to learning, unlike today's PhD programs in which students are embedded in one lab and obtain highly specialized educations. The professors were terrific, and we were required to take courses and exams in ecological genetics, population genetics, human genetics, quantitative genetics, molecular genetics, and biochemistry, among others. I recall studying six months for my PhD exams, which had written and oral components. Looking back, I obtained an amazing breadth of genetics knowledge that helped me immensely when I started my own lab and began teaching introductory genetics to undergraduates as a young faculty member.

I immediately settled into Albert's lab that he shared with his colleague and collaborator, Milt Zaitlin. At the time, the lab had about 20 graduate students, postdocs, and technicians. Milt received his PhD at UCLA from Sam Wildman, who was one of "founders" of plant molecular biology and discovered RuBP Carboxylase—the most abundant protein on the face of the earth. Ironically, I would replace Sam at UCLA when he retired in 1976. I was hired as a young assistant professor, ten years in the future. My new research home was the largest and most highly funded research lab on the U of A campus and unlike any that I worked in at OU. Albert and Milt were carrying out pioneering experiments that eventually uncovered the mechanisms of virus RNA replication in plant cells. My first project was to determine the effects of a chemical, semicarbazide, on tobacco mosaic virus (TMV) replication, following my undergraduate interests in mutagen research. This ended up as my master's degree research which was required of all students before embarking on their PhD. I was exposed to a new world of science possibilities and introduced to all the cutting-edge instruments used to investigate plant cell processes of that era. The lab was a "playground" to explore all the latest methods and techniques to uncover the mysteries of plant cells. We even had the most sophisticated and expensive equipment of the day, a Model E Analytical Ultracentrifuge—a large "Buck Rogers" like machine that took up a small room and allowed you to measure the density and sedimentation velocity rates of macromolecules in real time. It was the same machine that Meselson and Stahl used to uncover the mechanism of DNA replication at Caltech. Today,

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an equivalent centrifuge costs ~$500,000! We also had our own greenhouse complex. I learned how to grow and nurture tobacco plants that were used in the lab for all our experiments. This would become the focus of my early experiments as an independent investigator in the future. Albert and Milt were inspiring professors and became life-long mentors and friends, until they both passed away several years ago. Most importantly, working in their lab reinforced my fascination with plants and helped catalyze my interests in science. I knew then that I had taken the correct career path. What could be better than a life of teaching genetics and carrying out plant research!

My graduate studies were proceeding smoothly, and I was making excellent progress on my TMV project and fulfilling my course requirements. The genetic code was cracked at the end of 1966, and we now understood how genes programmed the production of specific proteins—a spectacular advance in our understanding of cell processes. It was an exciting time, and I couldn't wait to read about the latest breakthroughs in *Nature, Science,* and *PNAS* and present them in our lab journal club. During my second year at the U of A, however, I was blindsided by a disaster that made me question whether I would be able to go on in science and which affected my life to this very day. I came down with a debilitating demyelinating disease, called transverse myelitis. It was a side-effect of a common flu that I had just before Christmas, an unfortunate present from Santa. Transverse myelitis results from a one in a million chance of an antibody fighting the flu virus carrying an epitope that recognizes and destroys the myelin sheath surrounding the spinal cord leading to paralysis. I hit the jackpot in a disastrous way! I was hospitalized and completely paralyzed except for the ability to talk. I couldn't walk, use my hands, feed myself, or do anything without 24/7 help from the hospital staff. It was a very dark time as I had to ponder the question of whether I would live or remain in that state for the rest of my life. I was in uncharted territory. My family physician, Dr. Frank Plotkin, who had known me since I was a child, was a constant source of support and encouragement. Frank told me that he didn't know whether I would get better, but I could still think and communicate and, if necessary, direct others to carry out my ideas. Lying in that hospital bed unable to move, I became determined to resume my graduate studies and continue my dream of being a plant scientist, no matter how hard it might be...even if I had to do it from a wheelchair! Fortunately, after several months in the hospital I regained many, but not all, of the bodily functions I had lost. I learned how to move my arms and legs, stand up, and walk again with the help of hours and hours of physical and occupational therapy, functions that we take for granted since the time we are infants. Unfortunately, I permanently lost my ability to distinguish between hot and cold temperature over much of my body, extend the fingers of my left hand, and, more seriously for a budding scientist, the total use of my right hand, among many other complications. This was devastating for me and required many adjustments. How was I to write since I was right-handed? I decided that the best thing for me was to go back to school and focus on my science journey, even though I was a skeleton of my old self, needed more physical therapy, and had to learn to adjust to daily life with only one hand. Looking back, this was the defining moment of my entire life. Did I have the physical and mental strength to do it and overcome my physical disabilities? This was not an era of barrier-free design, rooms for the disabled, or sensitivity to individuals with disabilities. For better or for worse, you had to "suck it up" and make it on your own. I went back to the U of A and rejoined my lab. Albert and Milt were shocked by my physical transformation, and gave me much encouragement, support, and help. Adjusting to daily life and working in the lab with one hand were the hardest challenges I ever had to face. My lab mates were very supportive and never hesitated to help me put a rotor in the centrifuge, tie a dialysis bag, pot tobacco plants, or with countless other tasks that I couldn't do on my own. One of the most difficult challenges,

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however, was teaching myself how to write with my left hand. It was a very painful process that I still haven't mastered.

Two years later, in 1969, I completed my TMV research project and typed my Master's Thesis with one finger on an old electric Smith Corona typewriter, "The Effect of Semicarbazide on Tobacco Mosaic Virus." At about that time I learned of a new surgical procedure that could be used to transfer tendons from one's arm to the hand to restore grasping function. I flew to Los Angeles and was operated on in the Orthopedic Hospital, which is now part of UCLA Health by a pioneering hand surgeon, Dr. John Boyes, who developed the new tendon transplant procedure. When I woke up from surgery a miracle happened. I was able to move the fingers in my right hand for the first time in two years! I went back to Tucson and after several weeks of recuperation and physical therapy I was able to use my right hand to pick up a glass, butter toast, open a door, drive, and do many other things that were impossible before. Although I couldn't move my fingers individually, I regained 75% use of my right hand, and that's where it stands to this day. I still write with my left hand, if you can call it that. I can write on a white board with my right hand while I teach, and type with my left and right fingers quite rapidly on a PC. So much for "chicken scratch!" Looking back, I am not sure how I did it, but I wouldn't change that period of my life as it helped me be the individual, teacher, and scientist that I am today.

I was able to work in the lab "normally" after my hand operation and embarked on my doctoral research. I decided to move away from plant viruses and study plant DNA. Right after I returned to graduate school from my hiatus with transverse myelitis I took a fascinating quantitative genetics course from Professor Bill Bemis, a Cucurbit breeder. I became fascinated with the new DNA/DNA and DNA/RNA hybridization procedures that were being developed in the 1960s and decided to use DNA/DNA filter hybridization to compare the DNA of different Cucurbit species, including those giving rise to pumpkins. Working with plant DNA in that era was a difficult, if not impossible task, and the few of us studying plant DNA had to invent purification methods "on the fly." I had to grind up kilograms of leaf material to obtain a few micrograms of Cucurbit DNA for my hybridization studies. However, this was the beginning of my five-decade "love affair" with plant genomes. I completed my PhD research in 1971, typed my thesis with two fingers on an old electric typewriter, and published my first paper in the journal *Genetics* shortly thereafter, "Nucleic Acid Hybridization Studies Within the Genus Cucurbita," with Albert and Bill Bemis as co-authors. From then on, I knew that a research career in science was a definite possibility.

What was my next step? In 1968 and 1969 two seminal papers were published in *Science.* The first, by Roy Britten and David Kohne, described the use of DNA reassociation studies to dissect the organization and evolution of eukaryotic genomes. Looking back, this ushered in the genomics era. Roy was a brilliant ex-physicist who discovered that eukaryotic genomes had repetitive DNA sequences. His *Science* paper, "Repeated Sequences in DNA," was a *tour de force* and described for the first time how eukaryotic repetitive and single copy DNA sequences were organized on a whole genome basis and how complex eukaryotic genomes might have evolved. The principles put forth in that visionary paper have stood the test of time and have been validated by the whole genome sequences of hundreds of different animals and plants. The second paper, by Roy Britten and Eric Davidson, "Gene Regulation in Higher Cells: A Theory," provided a hypothesis for how thousands of eukaryotic genes could be expressed coordinately in space and time to drive the complex process of eukaryotic development. Simply put, this paper provided the conceptual basis for what we now call "gene regulatory networks," or GRNs, that are the focus of much genomics research today. Eric became one of the most influential animal developmental biologists of the modern era and was an iconic figure in elucidating eukaryotic developmental-specific regulatory processes. I was very struck by the importance

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of these two papers, although not understanding them completely, and realized that they provided a road map for how to dissect the molecular basis of plant developmental processes in the future. I also knew, personally, the limitations of molecular plant research at that time and felt that I could learn a lot by switching to animal systems. In the summer of 1969, I took a risk and wrote to Eric, who was at the Rockefeller Institute at that time, about the possibility of joining his lab as a postdoc. I didn't think I would obtain a response being a graduate student working on plants in an obscure university in the desert. However, I had nothing to lose and several weeks later I received a letter from Eric inviting me for an interview in New York. As it turned out, this became one of the most consequential events in my entire research career. Eric was very intimidating and the most brilliant individual that I had met up to that time. There was nothing that he didn't know, and he peppered me with questions about my PhD research. After five or ten minutes he said, "these are the dumbest experiments that I have ever heard of. Why are you wasting your time on pumpkin DNA?!" He then thanked me for flying to New York to see him, said good-bye, and walked out of his office. I flew back to Tucson after my short interview and told Albert and Milt that "I am not going to get that postdoc in a million years." Two weeks later I was shocked to receive a letter from Eric offering me a postdoc position and indicating that he was moving to Caltech in Pasadena to set up a new lab to investigate animal development and Roy Britten was joining him. I hit the jackpot. I was going to postdoc with the two most influential scientists working on eukaryotic gene regulation and genome organization at that time!! I applied for a NIH Postdoctoral Fellowship and was awarded my first grant on a competitive basis, and in the fall of 1971 drove across the desert to Los Angeles to join Eric's lab. Hollywood here I come!!

I rented a small house in Laurel Canyon, an iconic area in Hollywood above the Sunset Strip and about 10 miles from Pasadena. Frank Zappa had a house down the street. The Canyon Store, which is still there, was a gathering place for budding 1970s musicians such as Joni Mitchell, Carol King, and John Mayall. It was a magical time. I fell in love with Los Angeles, where I have now lived for over 50 years. Caltech was an amazing intellectually vibrant place, unlike anything that I had experienced as a student at OU or the U of A. Ironically, next to my new lab was Max Delbruck's office, Albert's doctoral research advisor. Max won a Nobel Prize for developing bacteriophages as a system to study genes and recommended James Watson for a fellowship at Kings College where he would contribute to discovering the Double Helix along with Francis Crick, Maurice Wilkins, and Rosaland Franklin. Max would often pepper me with questions about what I was doing in the lab. At times he would mimic Eric and say "those are the stupidest ideas I ever heard"—a humbling but thought provoking experience. Down the hall was Lee Hood, a young assistant professor would go on to invent the DNA sequencing machine. Around the corner was James Bonner, who was an icon and pioneer in plant molecular biology. Upstairs was another Nobel Laureate, Ed Lewis, a fly geneticist who discovered homeotic genes. There was no shortage of brilliant individuals and exciting research labs to interact with and learn from. Eric's lab was a beehive of activity investigating the organization of animal genomes and how they were regulated during development, focusing on toads and sea urchins. I stayed away from the lab on days that DNA was extracted from toad blood, a gruesome Guillotine-like method that reinforced my previous choice to focus on plants and major in botany as an undergraduate at OU. The techniques of DNA/DNA and DNA/RNA hybridization were cutting edge and orders of magnitude more sophisticated than the primitive filter hybridization studies I was using as a graduate student. Roy lived on a boat and was located at Caltech's Marine Biology Lab in Corona Del Mar near Irvine 50 miles to the south. He would spend one day a week at Caltech and participate in our lab meetings, which were intense, critical, and, at times, above

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my head. If you didn't have "thick skin" you wouldn't survive. It was a "take no prisoner" approach. In fact, sometimes it took me days to decipher the ideas that were discussed in those lab meetings. I always had to be on my toes, as every experiment and thought was challenged by Eric and Roy. Those gatherings taught me how to think critically and dissect every idea I had and experiment that I carried out. Our lab was carrying out pioneering experiments and took the lead in developing new technology for dissecting eukaryotic genomes that laid the groundwork for the field we now call genomics. My postdoctoral project was to answer the question of whether sea urchin embryo polysomal mRNA was primarily transcribed from single copy sequences in the genome using DNA-excess DNA/RNA hybridization procedures. The answer was a resounding "yes." In 1973, I published a paper in *PNAS*, "Non-Repetitive DNA Sequence Representation in Sea Urchin Messenger RNA," with Eric, Roy, and Glen Galau, a graduate student in the lab who taught me many techniques, as authors.

I learned an enormous amount from Eric and Roy, and the concepts and techniques on how to investigate eukaryotic genome organization and expression provided the foundation for all my early work as an independent researcher, particularly my experiments in the pre-recombinant DNA era. Roy passed away at the age of 93 in 2012. He provided much critical advice when I was using the DNA reassociation techniques he invented to dissect plant genomes in the 1970s. Eric became a lifelong friend and inspiration until he passed away at the age of 77 in 2014. Before Eric passed away, he read one of my recent grant proposals and said "you are not going to send in this pile of junk?" Some things never changed! Nevertheless, he gave me terrific ideas on how to make the proposal better, as always, and it was funded.

In 1973, towards the end of my NIH Fellowship, Albert called me and said that he was moving from Tucson to set up a new Biology Department at Wayne State University in Detroit and wondered if I would like a job as an assistant professor? At the time, jobs in academia were scarce and, although I didn't like the idea of moving back to the Midwest, Albert gave me an amazing startup package that allowed me to set up my own state-of-the art lab and jump start my career as a professor and independent scientist. I immediately combined what I had learned about plants as a graduate student at the U of A and the sophisticated DNA and RNA hybridization techniques to study eukaryotic genomes at Caltech. The initial questions being, how are plant genomes organized and how are genes regulated in plant development, using tobacco as my model system. At the time, these were cutting edge questions and the experiments my lab carried out helped usher in the plant genomics era. I obtained my first NSF grant in 1975 on the organization and expression of plant genomes. Fortunately, I am still funded by NSF to this very day. I stayed at Wayne State until 1976 when a job opened for a plant developmental biologist in the Biology Department at UCLA... my dream job! I moved back to Los Angeles, climbed the academic ranks from assistant professor to distinguished professor. I met the love of my life, Michele Evans, who became my wife, and helped to raise three wonderful children: Ty, Aaron, and Makenna. I've had a "Cinderella-like" career for 50 years. I'm now the oldest active professor in the Life Sciences at UCLA, still trying to uncover the mysteries of plant genomes! Looking back, I wouldn't have changed a thing.

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

I established my own research and teaching program in 1973 during a period of great social unrest. The Vietnam War was raging, anti-war protests were occurring across the U.S. The Watergate Scandal was dominating the news and led eventually to the resignation of President Nixon. This was also the year in which one of the most revolutionary breakthroughs in the history of biology was reported. The demonstration by Paul Berg, Herbert Boyer, and Stanley Cohen that DNA segments of two different species could be combined and

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made to function in living cells. This made it possible for the first time to isolate, study, and recombine genes from any organism on the face of the earth, including plants. Genetic engineering and recombinant DNA technology were born! My lab and thousands like it across the globe would eventually use this technology to peel back the mysteries of how genes functioned and produce a mountain of new information about basic cellular processes. My career in science paralleled step by step the transition from the pre-recombinant DNA era through the development of the advanced genetic engineering and genomics technology of today.

This was also a time when teaching undergraduates at major research universities, such as UCLA, was not emphasized, or even valued, like it is today. What mattered most was how many papers were published and how much grant money was obtained to run your lab—helping, indirectly, to fill the university's coffers. The digital era had not begun, and the most advanced teaching tools were an overhead projector that projected hand-made drawings onto a screen and the Xerox machine which allowed copies to be made of your exams, replacing the old-fashioned Mimeograph. In the classroom, most professors hid behind podiums, read from their old notes on faded yellow legal pads, scribbled with white chalk on dusty blackboards, and babbled on in monotone during their lectures putting their students to sleep. No wonder why so many students were turned off to science! It is from this perspective that I have made my most important contribution to science over these past decades, teaching thousands of undergraduates—both science and non-science students—that science is exciting, inspirational, and relevant to their lives.

I always looked at the classroom as a "laboratory" to develop new methods and approaches to teach and make large classes personal, interactive, and conceptual—analogous to the wonderful classroom experiences I had as an undergraduate at OU. I initiated many innovations in the classroom which were considered radical, or even blasphemous, at a time when undergraduate teaching was an afterthought. Many of these innovations I use to the present day, although with digital media and a renaissance in college teaching some have become "mainstream." I rebelled (once again) from the norm of the day and went against the "rules" of my department which almost cost me my dream job at UCLA in the early 1970s. I refused to grade on a curve which was required by the Biology Department in that era and, in my opinion, a race "to the bottom." I initiated a collaborative learning environment in which students interacted on take-home exams and were told if they learned what I asked them to learn conceptually they would be rewarded and get the grades they earned without competition from others. "Here's what is important to learn and if you learn the concepts you will succeed!" To guard against potential cheating, I initiated all-class oral exams in which student groups answered take-home exam questions before the entire class and were "penalized" if they couldn't provide the conceptual answers that they wrote on their take-home exams. I took polaroid pictures of all students in the class and called on them randomly during the quarter to answer challenging questions in class—an approach that 40 years later is called "active learning." I used reel-to-reel films in the "old days" (e.g., "Race for the Double Helix", "Inherit the Wind", among others) to bring science alive and show how it affects our lives and carried out simple "experiments" in the classroom such as spooling DNA out of solution. I also took all the students out for lunch or dinner in large groups to get them to "know the professor" and make a large class more personal. I focused on the concepts, experiments, and people that made the major breakthroughs, in order to introduce students to exciting discoveries and how they were made. In the early 1990s, I started using undergraduates as teaching assistants to teach Socratic-style discussion sections in my classes. These were students who had taken my class previously and showed potential for being terrific teachers. I initiated a seminar course called "Teaching Students How to Teach" that guided

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these undergraduates on how to become teachers. I also initiated new "whole campus" science classes designed for non-science majors when major scientific advances occurred to educate these students on the importance of these "revolutions" in their lives, courses such as: The Human Genome, Genetic Engineering, and my current course, Genetic Engineering in Medicine, Agriculture, and the Law, which merges the political science background I obtained from my OU undergraduate days with contemporary genetic engineering and genomics discoveries and their effect on society. When the digital era was born, I took advantage of the internet by incorporating students from other universities into my UCLA classes (e.g., Kyoto University in Japan) and created some of the first long-distance learning environments establishing a novel cross-cultural education experience for the students involved. Finally, I collaborated with the UCLA School of Film, Television, and Theater to create an interactive version of my genetic engineering class—animating every conceptual process analogous to a "Disney-like" documentary. In the beginning, many of my methods broke the norms of the day, got me into trouble with my deans and department chairs because they were not understood. Although it was hard swimming against the current for so many years, I am happy that many of my methods are now mainstream and that I managed to open new vistas for thousands of science and non-science students, including children of many former students!

What about my research trajectory? One of the dreams every scientist has is to translate discoveries made in their laboratory into real applications that benefit society. For myself that means taking discoveries from the "test tube to the farm." One of my most significant contributions to the plant sciences is to have uncovered genes important for pollen formation and using their control elements and fascinating bacterial defense genes to genetically engineer for male fertility control—establishing a new "breeding system" for generating hybrid canola plants—which are now the dominant commercial varieties grown in Canada and many other parts of the world with a significant increase in oil production. This story began in the late 1970s and early 1980s when my laboratory carried out a series of novel experiments to answer the question of how many genes are expressed in plant cells and what is the extent to which genes are regulated during plant development. In that era little was known about plant genetic processes at the molecular level. To answer these questions, we used the DNA/RNA hybridization studies that I learned when I was in Eric's lab at Caltech—techniques that were cutting edge and designed to quantitate gene expression profiles on a whole genome basis—that is, they were the forerunner of the advanced genomics techniques of the current day. With the help of a former graduate student, Joe Kamalay, and my first lab technician, Gisela Hoschek, we hybridized an excess of tobacco leaf polysomal and nuclear RNAs with radioactive tobacco single-copy DNA that we had isolated from the tobacco genome by DNA/DNA reassociation fractionation. We showed for the first time that there are ~30,000 genes expressed in a plant organ system, and that plant cells have complex nuclear RNA sequences (i.e., HnRNA) analogous to those in metazoans, indicating that gene expression processes in plants and animals are similar even though they are separated by one billion years! When the recombinant DNA era began it was learned that the additional nuclear RNA sequences were primarily, although not exclusively, derived from introns in plant genes. We next tackled the question of how many genes are required to program plant development and the extent to which genes are regulated in vegetative and reproductive organ systems. In a series of technically difficult experiments carried out primarily by Joe, we used DNA/RNA hybridization to purify two labeled single-copy DNA fractions: (i) one complementary to tobacco leaf polysomal mRNA sequences, designated as leaf mDNA (i.e., gene sequences active in the leaf) and (ii) the other devoid of leaf mRNA sequences called Null mDNA (i.e., all other genomic sequences includ-

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ing genes active in other parts of the plant). We then hybridized the labeled single copy leaf mDNA and Null mDNA fractions with an excess of polysomal mRNAs from leaves, stems, roots, petals, pistils, and stamens to saturation. The results demonstrated that each organ system had a unique set of genes expressed exclusively in that organ, and that at least 60,000 diverse genes are required to program plant development. At that time, this was a controversial number and when I first presented the results during a lecture at the Edinburgh Plant Genome and Organization Meeting in 1978 a participant in the audience shouted, "Goldberg is full of s--t, everyone knows there are only 5,000 genes expressed in a plant cell similar to those in bacteria!" I pushed back strongly and explained that most plant genes encode rare mRNAs that don't direct the synthesis of enough protein to be visualized on the protein gel electrophoresis systems of that day which underestimate the number of active genes by an order of magnitude. Remarkably, the gene numbers we obtained from our "primitive" DNA/RNA hybridization experiments have stood the test of time and are consistent with gene numbers obtained from direct sequencing and transcriptome analyses of plant genomes. In a complementary series of experiments, we separated labeled single-copy DNA enriched for sequences complementary to leaf nuclear RNA (leaf HnDNA) from those devoid of these sequences (Null HnDNA) and hybridized both single-copy probes with excess leaf, stem, root, petal, pistil, and stamen nuclear RNAs. The results showed that each organ system has a unique set of nuclear RNAs mirroring our results with polysomal RNAs, and that genes encoding these organ-specific RNAs are primarily under transcriptional control, although post-transcriptional processes were also shown to play a role. We published the results of these experiments in three papers—two in *Cell* and one in *PNAS*. In that era, like today, *Cell* only published papers that had a high impact on their fields, and our two tobacco gene expression papers were "pioneers" and among the first plant papers ever to be published in that journal. Although they are now over 40 years old, and, sadly Joe and Gisela, are no longer with us, our results have stood the test of time and were the forerunners to the RNA-Seq genomics experiments of the present day using both nuclear and cytoplasmic RNAs (i.e., mRNA-Seq and nuclear RNA-Seq).

The recombinant DNA era became mainstream during the late 1970s and early 1980s when we were carrying out our DNA/RNA hybridization experiments. I was fortunate in that Winston Salser, who invented cDNA cloning along with Tom Maniatis at Harvard, had the lab next to mine in the old Life Sciences Building at UCLA. Winston's lab had purified all the enzymes required to clone mRNAs (e.g., reverse transcriptase, S1 nuclease, DNA polymerase) and had the expertise to insert cDNAs into bacterial cells using plasmid vectors—techniques that were new to those of us working with plants. Although now retired, Winston was one of the founders of Amgen which is now one of the largest biotech companies in the world. With the help from Winston's laboratory, my technician at the time, Jessie Truettner, and I set out to clone the mRNAs that were specific to each tobacco organ system to begin to determine how they were regulated in development. We uncovered a number of anther-specific cDNA clones and used *in situ* hybridization techniques that were developed for plants in my laboratory by a postdoc, Kathleen Cox, to show that many were specific for mRNAs localized exclusively in the tapetal layer of tobacco anthers. This tissue layer is essential for pollen formation and male fertility, and at the time were cutting-edge experiments because very few labs had uncovered genes with such developmental specificity.

One notable cDNA, which we designated as TA29 (Tobacco Anther cDNA Number 29), played a central role in very exciting experiments I carried out in collaboration with my friends, Titti Mariani and Jan Leemans, to engineer for male fertility control in crop plants and generate a new system for generating hybrid plants. Titti and Jan were scientists at Plant

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Genetic Systems (PGS) in Ghent, Belgium—an innovative plant biotech start up in the late 1980s and early 1990s that held some of the most important patents in plant biotech at that time—enabling technology for *Agrobacterium* transformation of plant cells as well as genetic engineering for herbicide and insect resistance. Jan is now retired, and Titti is the Head of the Department of Molecular Plant Physiology at Radboud University in The Netherlands. I was asked to be on the PGS Science Board, and we brainstormed how the anther-specific *TA29* gene uncovered in my lab could be used to engineer for male sterility which is important in breeding hybrid crops that have higher yields than their non-hybrid relatives. In the 1920s Henry Wallace, who became Vice President of the United States under President Franklin Roosevelt, invented a method to breed for hybrid corn and started an agricultural revolution that became the foundation of the commercial corn industry to the present time. Wallace's method requires the use of a male sterile line to make a directed cross between two inbred varieties yielding hybrid seed. This is done by mechanically "emasculating" one corn line and using it as the female line in a cross with another variety that is male fertile. Although costly, this works well with corn because tassels containing the anthers are large and relatively easy to remove from the plant. However, many crops, such as canola, have small flowers and mechanical removal of the anthers is not possible on a large-scale commercial basis. At the time, PGS was using two proteins, barnase and barstar, from the bacteria *Bacillus amyloliquifaciens* to study protein structure and interactions. Barnase is a small RNase that is secreted by the bacteria as a defense mechanism to protect it from predators. Barstar, on the other hand, is a RNase-inhibitor that binds to barnase in the event it is retained in bacterial cells; that is, a failsafe agent that protects the bacteria from being destroyed by its own RNase. In my laboratory at UCLA, Jessie and I isolated the *TA29* gene from a tobacco genomic library and two postdocs, Kathleen Cox and Anna Koltunow, carried out promoter analyses to uncover the region responsible for regulating the *TA29* gene exclusively in the anther. Jan and Titti, and their colleagues at PGS, fused the *TA29* gene control region to the *barnase* gene and transformed the chimeric *TA29/barnase* gene into both tobacco and canola plants. Much to our surprise and excitement barnase was produced exclusively in the anthers of both plants, destroyed their tapetal layers, and generated 100% male sterile plants that were otherwise perfectly healthy. We then constructed a chimeric *TA29/barstar* gene and inserted it into tobacco and canola plants. As predicted, the *barstar* gene was expressed only in the anthers and the transformed plants were male fertile. Crossing the male sterile barnase plants with the male fertile barstar plants generated fertile hybrid offspring demonstrating that we could engineer for male sterility and restore fertility using our chimeric *TA29/barnase* and *TA29/barstar* genes. We published these results in two *Nature* papers in 1990 and 1992, and PGS then set out to commercialize our system to generate hybrid canola seeds—which did not exist at that time. After going through an extensive breeding and regulatory oversight, the first commercial hybrid canola seeds were sold in 1996 to farmers in Canada. These seeds had a significant increase in oil content compared with existing non-hybrid canola varieties. Fast forward to the present day, hybrid canola seeds using the *TA29* barnase-barstar system now represent greater than 50% of the Canadian canola seed market, and over 20 million acres of canola with our *TA29* gene promoter are grown annually in Canada and other parts of the world. This is one of the most successful first generation "GMO" stories along with herbicide-, insect-, and viral-resistant plants – and represents true translational agriculture in going from the laboratory to the field. PGS was sold in 1996 for almost $1B, I built my dream house in Topanga Canyon, and TA29 is now the license plate on my car! When I first started my own laboratory, I could not have imagined making a significant impact on seeds planted by farmers in their fields. A scientist's dream come true!

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There is one other important contribution to the plant sciences, among many, I would like to mention briefly, and which played a major role in my career. While we were carrying out our tobacco gene expression studies in the late 1970s, I carried out a series of experiments on soybean genome organization and gene expression during seed development using DNA/DNA reassociation and DNA/RNA hybridization methods. I was asked by Bill Briedenbach, now a retired UC Davis Professor, to collaborate on a project to clone soybean seed protein genes and study their expression during development – thus, began a career-long journey in unraveling the processes that control seed and embryo development in higher plants that continues to this day.

I was very fortunate at that time to have a large number of outstanding students and postdocs who took on the task of isolating and investigating different seed protein genes, such as those encoding glycinin, β-conglycinin, and Kunitz trypsin inhibitor, among others. These included Bob Fischer, John Harada, Linda Walling, Jack Okamuro, and Diane Jofuku all of whom went on to significant independent careers in the plant sciences. I was struck by my interactions with scientists at PGS, particularly how collaborations with individuals having complementary expertise could make important scientific advances, as compared with the "single lab" model that was prevalent in the biological sciences at that time. In fact, because of the way academic promotions were made, large-scale collaborations were frowned upon (e.g., who was responsible for that idea?). Fortunately, the genomics era swept away the "single-lab" approach to science and spawned large-scale collaborations that have been pushing back the frontiers of science. However, this was new as the dawn of genomics approached in the late 1980s and early 1990s. I organized a meeting at UCLA in the Fall of 1989 with many of my former students and postdocs and proposed a scientific collaboration, called the Embryo 21st Century Project, to identify and study "all of the genes required to make a seed." This goal, of course, turned out to be more complex and challenging than we imagined at the time, but began an exciting collaboration that lasted for over 30 years. In fact, the retreats we had each year at the UCLA Conference Center in Lake Arrowhead from 1990 to 2020 became, arguably, one of the longest standing plant embryo meetings and provided a novel gathering of PIs, postdocs, students, and technicians to discuss their most recent embryo research. At its peak, over 60 individuals attended each year over a three-day weekend. After PGS was sold in the mid-1990s I started a biotech company with a friend of mine, Walter De Logi, who was the CEO of PGS, and a colleague of his, Ned Olivier, who had a venture capital firm that funded many of the new human genome sequencing startups of that era. The idea was to have a company, Ceres, that would translate basic science discoveries into important practical advances in agriculture and an institute, called the Seed Institute, that would make fundamental discoveries in how seeds develop—morphing the Embryo 21st Century Project into the Seed Institute. As part of this venture, Ceres provided $10M in funding for the Seed Institute which was distributed to individual labs in the UC (Bob Fischer, UC Berkeley, John Harada, UC Davis, myself, UCLA) and University of Utah (Gary Drews). This took an enormous amount of energy as it required writing "new rules" for university-company collaborations. However, fast forward to the present day several novel discoveries regarding seed development were made by the Seed Institute collaboration – all of which were published collectively by Seed Institute investigators. These include the mechanism of imprinting in higher plants by experiments carried out primarily in Bob Fischer's lab, the identification of LEAFY COTYLEDON (LEC) as a major regulator of seed development spearheaded by John Harada's lab, and an atlas of gene activity in every seed organ, tissue, and cell type carried out by John Harada and my lab, among others. Gary, Bob, and John are now retired, although John and I continue our Seed Institute collaborations, yet I suspect that I will be the "last man standing" and will need to be pried loose from the lab bench when a journey beginning 60 years ago as an undergraduate botany major

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finally comes to an end – whenever that will be. Finally, I would like to acknowledge all the wonderful individuals, only a few who have been mentioned here, who helped me make my career in science an unpredictable success, as I could have never accomplished what I have been able to do in the classroom and laboratory without their dedication, help, and friendship. It was a "family" effort. Thank you!

When did you become a member of ASPP/ASPB?

I was not active in the ASPP/ASPB during the first part of my career. Most of the meetings I went to in those days were multidisciplinary, such as the Annual Genetics Society Meeting or the Developmental Biology Gordon Conference, among others. In addition, my early publications were in multidisciplinary journals as well—*Genetics, Developmental Biology, Cell, PNAS*—as that was the audience I wanted to reach. I became active in the ASPP/ASPB when Charlie Arntzen then President of the ASPP, asked me to start a new journal for the Society which became *The Plant Cell*. Up to that time I was an "outsider" to the Society and hadn't participated in any of the Society's activities, including going to annual meetings and publishing in its then "flagship" journal, *Plant Physiology*. I will not dwell too much on how I started *The Plant Cell* as I have written extensive editorials on the history of the journal on the 20th and 30th anniversaries of its founding in 1989. However, that's when I became a member of the ASPP/ASPB.

After stepping down as founding editor of *The Plant Cell*, I turned my focus back to teaching and my research on seed development. I was re-connected with the Society when I was asked to be on the ASPP/ASPB Education Foundation and to make a documentary film that educated the public on the importance of GMOs in agriculture—countering the anti-GMO propaganda that was prevalent in the late 1990s to the mid-2000's. I found a wonderful producer, Martin Durkin, who had made several science-oriented documentaries, and we made a film,*"History's Harvest: Where Food Comes From,*" which took about two years of my life to make. I reluctantly agreed to be the narrator of the film (at Martin's insistence), and we went to several places around the globe (e.g., India, Mexico, England) interviewing scientists on the origins of agriculture and the influence of classical genetics and genetic engineering on increasing food production and generating new varieties of higher yielding crops. This film has been shown widely to diverse audiences and can be viewed currently on YouTube and/or a DVD that can be obtained from the ASPB.

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

Francis Crick once said to me "if you are the smartest person in the room, you are in trouble!" It is critical to always reach for new horizons and to seek out individuals that are smarter than you and from whom you can learn. I have followed this advice since I had my "five minute" interview with Eric Davidson for a postdoc position in 1969 until the present day, and it has been one of the guiding principles of my career. Follow your heart even if you have to swim "upstream," don't be intimidated by prevailing rules, and rebel against the current dogma, if necessary, in order to make major advances in science and teaching. Finally, have fun!