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My Secret Life

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Abstract

In my early childhood, my parents gave me to my maternal grandparents for a "visit" that extended over a period of nine years. I seemed to be a fairly ordinary student in primary grades, and had to take a remedial general science class upon entering high school, my first exposure to science. It was the teacher of that class, Mr. Auer, who told me that I had scored amazingly high on a science aptitude test given to all freshmen. The people who administered the testing were convinced that I must have cheated somehow. Mr. Auer suggested that I might want to consider a career in science if I liked it. I loved it, and I did. This autobiographical article recounts my changing interests as I became aware of new fields of science during my education and the start of my career. Out of basic studies of a microbe that causes plant cancer, we developed a method to engineer new and useful genes into crop plants.

Contents

PROLOGUE

When I was a youngster, I was just an ordinary kid. There was no hint of the curious student or the competitive scientist who would eventually emerge. I galloped around pretending to be a horse. I dug holes. I climbed trees. I had little use for dolls or ruffles. I was a tomboy. It may seem of little

value to start a scientist's autobiography at birth, to bring up events that predate even my first memories. But early events can be formative, and I had an unusual childhood. I ultimately became a driven person, and I have often been asked about what the source of that drive was. Truthfully, I do not know, but it must have started early. In that spirit, I invite you to come along and look back with me. Perhaps we will notice some clues.

I AM NAMED MARY DELL

I was born in 1939 on one of our lesser holidays, Groundhog Day, an unplanned addition to a family of two handsome blond-headed brothers. Family legend has it that when the nurse brought infant me, with my mop of black hair, to my mother's bedside, she took one look and declared, "She's not mine! Take her away!" Nevertheless, she was persuaded to accept me, and indeed she gave me my first gift, her own name, Mary Dell. Because our names were otherwise identical, I was, in full, Mary Dell Matchett II. The roman numeral appended to my name, when I became old enough to read it, made me prideful, with its ring of royalty or papacy.

A hyphen between Mary and Dell was a second gift from my mother years later. She became furious because my fifth-grade teacher called me Mary. She huffed, "That is *not* your name!" and renamed me Mary-Dell, to clarify that it is a double first name. When I became a teenager, my mother admitted to me that she did not like women in general. When she was confronted with the problem of a girl baby requiring a name, there were no women's names that she liked—except her own. I suppose it is not surprising that she chose her own name for me. Whatever her reason, I am grateful to my mother for my given name, hyphen and all. A part of that name came from her mother, as we will learn next.

I MEET MY NANNAN

When I was about three, we had a visitation by my maternal grandmother, Henrietta Dell Hayes, whom we were instructed to call Nannan. She was nice, but it was hard to talk with her because (my mother told us) she was "death." That scary word meant that she couldn't hear unless she wore her hearing aids. Nannan showed me the big batteries the size of hot dogs that she wore in a silk packet on her leg. They were wired to little boxes hooked to her corset. Each box sent sounds through a fine wire to one of the ear tips, which had been molded to fit each of her ears. With these little machines switched on, she could hear pretty well. Without them, she was stone "death": You could make all the racket you wanted to and, amazingly, she heard nothing!

After a few days, Nannan asked me if I would go home with her to North Carolina to meet my grandfather, Daddy Hayes. I must have liked this idea, perhaps surprisingly, for such a young child. I think I was more fearful of staying than going. It offered an escape from my five-year-old brother, Bob. From the time I was an infant, Bob was a constant danger to me. I was terrified of him. My mother lamented that she did not dare to leave me alone in the house with Bob. I suspect that this was a major reason they let Nannan take me to North Carolina for a "visit" that was to extend over a period of nine years.

DADDY HAYES

My earliest conscious visual memory is of my small self, standing on the train platform in Southern Pines, North Carolina. My Nannan was behind me, pointing toward a tall stranger, saying, "That's Daddy Hayes! Run and give him a big hug!" which I obediently did. He was to become my best friend. Claude L. Hayes, my Daddy Hayes, owned Hayes' Book Store on Broad Street (see **Figure 1**), and introduced me to *Alice in Wonderland*, *The Wind in the Willows*,

Figure 1

Photograph taken at Hayes' Book Store during (I think) its 50th anniversary sale and celebration. Each customer was given a free pair of nylon stockings, which at that time were like gold. From left to right: my cousin Ray Hayes; his mother, Edna Carter Hayes (Aunt Ed); a family friend hiding in the back; my maternal grandfather, Claude L. Hayes (Daddy Hayes); his wife, my grandmother Henrietta Dell Hayes (Nannan); my mother, Mary Dell Matchett; and in front, my young self, Mary Dell Matchett II, wearing my favorite blue velveteen dress. (It was such a cold day, and photographers are so slow, that I had twined my legs together for warmth.)

Winnie-the-Pooh, and all of the children's classics. When I learned to read on my own, I devoured comic books. Daddy Hayes allowed me to take three at a time from his stock, keep them spotless, and turn them in for three more. I was the envy of my class at school. My next selections were dog stories and horse stories, followed shortly by the Nancy Drew mysteries and the Hardy Boys mysteries. To this day I am an avid reader of fiction, largely, I suspect, because of the early influence of Daddy Hayes and the many books he read to me.

NANNAN'S DRESS SHOP

Next door to the bookstore was Mrs. Hayes' Shop, owned and operated by Nannan. She wasn't just a sweet little old grandmother; my Nannan was a successful businesswoman! She went twice a year to New York City on buying trips. She sold elegant ladies' wear to the affluent tourists who came

to this winter resort area for golfing, tennis, and horseback riding. Nannan took pride in selling the first ready-made hats for fashionable ladies (who had, in past times, been obliged to create their own hats). She sometimes returned from New York with something for me. My favorite was a dark blue velveteen dress with a white lace collar (which I was wearing in the photo shown as **Figure 1**). Perhaps Nannan's work is what fostered the interest I would later have in apparel. Today, even though I live in a large metropolitan area, my face is familiar to the shopkeepers at the mall. I like to imagine that the spirit of Nannan cruises my favorite stores with me.

MY GRANDPARENTS' HOME

Southern Pines is a pleasant community, with many warm, sunny days in the wintertime. It was named for its beautiful longleaf pine trees, whose shining needles make the landscape green all year round. Nannan and Daddy Hayes lived in a big stucco house on a huge lot that extended from one corner to the next. They had a big lady named Dora who cooked breakfast and supper and got me off to school when I was old enough. Dora made the best sugar cookies I ever tasted, each with half a pecan baked in its center. Before I was old enough for kindergarten, when Nannan and Daddy Hayes went to work at their places of business, I trailed after one or the other of them and amused myself as best I could. The bookstore was a much more entertaining place than the dress shop, where you weren't allowed to play with anything. The bookstore was full of playthings: paper and pencils and paperclips and strings and elastic bands and stamps and ink pads. There was a long narrow office walled off at the back of the store, where my aunt Edna Carter Hayes, whom I knew as Aunt Ed, was in charge. The office had an immense mechanical calculator, huge ledger books with columns of figures that made no sense to me, and office chairs that could spin you around and around. Aunt Ed lived at Daddy Hayes's house too, in an upstairs bedroom. She had beautiful snow-white hair that she would let me brush sometimes. She braided it and wore the braids neatly wrapped around her head like a crown. I never knew her husband, my uncle Ray, who died before I was born and was never talked about. Aunt Ed explained to me that he was a soldier who died in the war.

Their son, my cousin Ray, lived with us at Daddy Hayes's house too, in another upstairs bedroom, when he wasn't away at college in Chapel Hill. He was the only grownup who wasn't old, and I loved having him home from school. He would lift me up so I could touch the ceiling and roughhouse with me and teach me important things, like how to slide down the banister and how to print my name. "How will your teacher know which paper is yours if you don't learn to write your name on it?" he challenged me. He explained some mysteries of the grownup world, like what Daddy Hayes really meant when he answered all of my "Where is my storybook?"–type questions with "Down cellar behind the axe!" (That meant "Don't ask me so many questions!")

CATHOLIC SCHOOL

My mother wanted me to have an "ordinary" childhood. She didn't want me to have things that other kids didn't have. That should have meant attending public school, but Daddy Hayes insisted that I go to private school. Notre Dame Academy was reputed to be the best in the community. The convent that housed the school was a long bus ride out into the country. Its teachers were nuns who wore strange long black habits with huge white bibs. Their hair was completely hidden by a black cloth. We were taught to call our teacher Sister Theresa Margaret, but the head of the convent was to be called Sister Superior. Very naughty children were sent to Sister Superior for discipline. There were two grades to a room. I remember penmanship as a difficult class in Catholic school. We had to use scratchy, blotty stick pens with sharp points that we dipped into

inkwells set into our desks. The nuns were excellent teachers who were strict but had a wealth of patience. I remember feeling like a very ordinary student. All students, Catholic or not, were required to pray a Litany after lunch each day, kneeling on the hard wooden seats of our desks. We reiterated our part—"Pray f'r'us!"—as quickly as possible in order to get our knees off those hard seats. We were praying for the end of the Litany.

HORSES, HORSES, HORSES

Absolutely the very best thing about living with my grandparents was horseback riding lessons. They were a bribe for taking piano lessons. My riding teacher, Mrs. Caddell, put me on a beautiful and absolutely reliable elderly black horse named Duke. Duke loved sugar cubes and carrots and little apples, which he munched eagerly. It tickled pleasantly when he licked the palm of your hand with his warm pink tongue. You had to put the treat on your palm and hold the hand quite flat so Duke could nibble sugar or apple but not fingers. I loved him with all my heart. He was the start of my first passion: riding, drawing, painting, and reading about horses, horses, horses!

MEDICAL ADVENTURES

When I was in third grade, eight years old, I awoke one night with an absolutely monstrous bellyache. I was barely able to creep from my cot in the den to the bedside of Daddy Hayes, wailing loudly. Nannan, of course, could hear nothing in the middle of the night without her hearing aids. Frightened at the sight of me, Daddy Hayes called his physician, Dr. Mac. I remember he asked Dr. Mac if it would be OK to give me a half of one of his codeine tablets. These were tiny pills about the size of Nannan's saccharin tablets, and it is hard to imagine how anyone could cut one in half, but he managed. Dr. Mac came to our house in the middle of the night, diagnosed appendicitis, and told Daddy Hayes to get me to the hospital.

The codeine must have put me to sleep. I awoke being wheeled into a room with a lot of lights shining on me and people in masks who were bent on doing bad things to me, and I remember screaming in terror. The next thing I remember is waking up in a dark room. I wasn't having any part of this place full of masked people with sharp things and bad intentions, and I carefully slid my legs out of the bed and headed for the door. A nurse caught me and inquired (reasonably enough, under the circumstances), "Where do you think you are you going?" I informed her with determination that I had decided not to have any operation. She said, "Oh, honey, you already had the operation! See?" and she hiked up my hospital gown to show me the biggest bandage I had ever seen.

I MEET MY MOTHER

Thankful that I had survived despite my mortal terror, I let her get me back into my bed. But when she announced brightly that my mother would be coming to see me later that day, I worried about how I would know her. I could not remember what my mother looked like. An even bigger worry was whether she would like me. Hoping that she might love me would be expecting far too much.

Later that day, Nannan came to see me, and with her was a beautiful lady who turned out to be my mother. She looked at me and beamed. She seemed to think I was OK, I thought. What a relief! She was nice! I do not remember much after that, but I was destined to become well acquainted with this beautiful mother of mine. She decided (based on absolutely no evidence known to me then or now) that the cause of appendicitis was eating too many cookies and not enough vegetables, a situation she decided to correct by taking me home with her and feeding me some "decent food."

I MEET MY BROTHER AGAIN

Gone were the horseback riding lessons, the comic books, the sugar cookies with half a pecan in the center. Gone were my beloved Nannan and Daddy Hayes. Gone were the longleaf pine trees with their shining green needles. Gone was the sunny winter resort climate.

My mother took me to Tess Corners, Wisconsin, to live with my two brothers and my father, who was home only on weekends. He traveled during the week, selling insurance. My father did not seem to like little kids much. My mother told us once, on a Monday when he had left for his week's work, "Your dad loves you the best in the world!" I did not doubt her words, but I remember being quite surprised. My oldest brother, Pete, commuted to Milwaukee on the train to attend high school. My other brother, Bob, still terrorized me. We went to the same school and were in the same classroom, which housed my third and Bob's fourth grade. My mother drove us the two miles to school and picked us up for the return to our rented farmhouse on Woods Road. On one occasion, she did not come to pick us up after school. We trudged home along the snowy road, but then found ourselves locked out of the house when we got there. Bob boosted me up to a bathroom window, which I managed to open and climb through. I was sorely tempted not to open the door to let him in. I made him promise not to hurt me. He did, and he kept his promise. It was the first time I had been of any use to him.

SUNDAY DINNER

Meat was expensive and money scarce, so my resourceful mother decided to raise a flock of chickens. She ordered a box of 100 chicks that spent the coldest nights in the kitchen. There was a henhouse in the backyard of our rented farmhouse that provided suitable housing for the birds in spring and summer. It eventually became Pete's job, axe in hand, to capture and murder our Sunday dinner. I remember being fascinated by the bright colors of the entrails of the chickens as my mother cleaned them at her kitchen sink. As I reflect on those times now, I imagine the culture shock for my mother, a southern belle reared at Daddy Hayes's dinner table. She had taught herself to cook. When times were hard, she learned how to raise chickens in order to provide for her family. My life has been easy compared with hers. Perhaps I gained strength from all of those vegetables she made me eat. But I prefer to think it was all that I learned from the good example of my resourceful mother.

A DEATH IN THE FAMILY

About a year after my return to my family, we learned that Daddy Hayes had become gravely ill. Leaving the rest of the family to cope, my mother and I drove to Southern Pines. It promised to be an extended visit, so I was returned to Notre Dame. Daddy Hayes needed more care and was placed in a nursing home. Christmas came and was scarcely noticed in our sad household. It was the only Christmas of my lifetime for which I received a single gift. I have a clear memory of the morning a few weeks later when Dr. Mac came to the house with bad news. Nannan did not have her hearing aids on yet. The doctor made a two-armed gesture of finality and told her, "It's all over." "Is he better?" Nannan asked hopefully. Dr. Mac shook his head and said, "He's gone." Nannan, who could read lips pretty well, got the message this time.

The death of Daddy Hayes brought changes to my life. Nannan was distraught and lonely. She really seemed to need me to stay with her in Southern Pines. It was decided that I would stay, a reprieve from the perils of living in the same house with Bob. My mother was now finally in a position to prevail on my schooling, and I was moved to public school at the start of fifth grade. That suited me, just as long as I could go horseback riding again.

FIFTH GRADE

The public school gave me a battery of placement tests to be sure I was capable of fifth-grade work. I was astonished when my teacher explained the meaning of the numbers in the report I was to take home to Nannan. For each subject, there were two numbers: The first was the grade level of my score, and the second was how many months into that grade I had achieved. My highest score was in reading (all those dog stories and horse stories!), where I scored somewhere in the 11th grade. In nearly every test, I had scored well above grade level, and my lowest score—history, as I recall—was somewhere in the middle of fifth grade. "Well, I guess they won't put me back a grade!" I said wryly to Nannan. "No," she said, "and your mother won't let you skip a grade, either." The results of these achievement tests astonished me. For the first time in my life, my tests were indicating that I was bright. I was 10 years old, half a year younger than most of my classmates, because I had started out in private school, where the rules about age were more flexible. The achievement tests fired something within me. It wasn't pride or arrogance. It was more like ambition. I started working. I stayed with Nannan in Southern Pines for two more years, spending fifth and sixth grades in public school.

CAMP AWA-NIKO

At about age 10, going to camp became a key piece of my life. In 1949, camp meant what kids now call "sleepaway camp": You went away from home and family, to the mountains if possible, to live with others your age in more or less primitive conditions. Nannan paid the tuition for me to go to the same small girls' camp, Awa-Niko, every summer for six years. The directors, Ruth White (Whitie) and Nancy Wrenn (Robin), were 29-year-old high school teachers who had met as WACs on Okinawa, the island for which their girls' camp would be named. They shared the dream of founding a girls' camp that they would build with their own hands. They made it all come true, adding one more cabin each year. They were fantastic people. I adored them. Camp was the best part of my youth. Nannan understood this about me. She said to me once, "You just *live* to go to camp every summer, don't you?" The experience of going to camp seemed to nourish a deep hunger in me, whose source we can guess if we allow ourselves to practice a bit of psychology without a license. Whitie and Robin paid attention to kids. For them, we weren't nuisances; we were treasures. Questions were encouraged. There was cooperation, conviviality, physical activity, and song. I was bonded not to the other campers but, rather, to these directors. Whitie once said about me, in my presence, "Whatever you're doing, she will suggest a better way to do it. And she's usually right!" That is one of two performance evaluations I have received in my lifetime that I still carry in my heart.

ABBOTT JUNIOR HIGH SCHOOL

When I was 12 years old, with puberty coming soon, my mother decided that I needed the influence of someone younger than a grandmother. I came back to my family, now living in Illinois, at the start of seventh grade. Seventh and eighth grades constituted junior high school, and mine, named Abbott Junior High School, had an excellent and enlightened curriculum. Both boys and girls were obliged to take cooking and sewing, and both were required to take woodshop and mechanical drawing. It was a great curriculum but for its one deficiency: It had no science class. There was a health class that covered medical topics quite well, but no science. This was to become a blessing in disguise later on.

During this time, our family, consisting of two parents, three children (two boys and me), and two dogs (a spaniel and a black lab), was living in a four-room house. My brothers had one

bedroom, my parents had the other, and I slept on the couch with the spaniel and lived out of the bottom drawer of my mother's dresser. My school wardrobe consisted of two corduroy suits, one green and the other red, that I wore to school on alternate weeks, and a couple of nylon sweaters to go with each. My mother washed out the week's suit in the kitchen sink each Sunday and hung it out on the clothesline to dry or freeze, depending on the weather. We really needed more room, and a washing machine.

HINSDALE TOWNSHIP HIGH SCHOOL

At this time, my parents built a three-bedroom house in Hinsdale, Illinois, a location chosen because it had one of the finest high schools in the west suburban Chicago area. I loved having a bedroom, and a bed. I also loved the high school. Because I had never taken a science class, my high school required me to take a remedial class called General Science. The teacher had the massive name Bastian Faginger-Auer, but luckily let us call him Mr. Auer. He was an absolutely superb teacher, and I became an enthusiastic student in his class.

SCIENTIFIC APTITUDE

My classmates and I were given a battery of aptitude tests in our freshman year, including one that was supposed to measure scientific aptitude. Mr. Auer asked me to come in and talk with him after school one day. Our discussion turned out to focus on my science aptitude test results. After inquiring whether I had ever before taken a test like that, he told me that the test administrators said that they could not believe my score. "Of course, they do not know you the way we do," Mr. Auer said, "but they were convinced you must have cheated somehow. They had never seen a score as high as yours." He suggested that I might want to consider a career in science, if it interested me. I was astonished. I absolutely had not cheated. The aptitude test had been fun and interesting, but to me, it had also seemed very challenging. I had no sense that I was particularly good at it. The advice of Mr. Auer may well have changed the course of my life, and I am eternally grateful to him.

MY NEMESIS, SKEETER

No description of my high school career would be complete without mention of my classmate Robert "Skeeter" Saunders, who was a nerd (though I do not think the term had been coined yet) at science and math. He was to challenge me throughout my high school career in those two fields. He was first and I was second at each contest, examination, or challenge of any kind. We were teammates on the Hinsdale team for the state math contest. Skeeter wanted me to be his girlfriend, but there was too sharp a stab of rivalry between us. Nevertheless, we served one another as worthy competitors throughout high school, and we have remained friends ever since. He later graduated from MIT and has now retired from a successful career in computer engineering.

MY FRIEND JOYCE

Another friend, Joyce, who attended a different high school, was exactly the opposite of Skeeter. She complained to me about how she was required to do a science fair project. I offered to help if she would let me pick the project, and she accepted my bargain. My choice was making a telescope. I ordered a kit from the Adler Planetarium in Chicago and received a nice letter from the director, Dr. Shatzel, inviting us to do the final stages of work—polishing and figuring our telescope mirror—in the optical shop at the planetarium. Eight months later, Joyce had a good grade and was long gone from the project, and I had a four-and-a-quarter-inch telescope mirror.

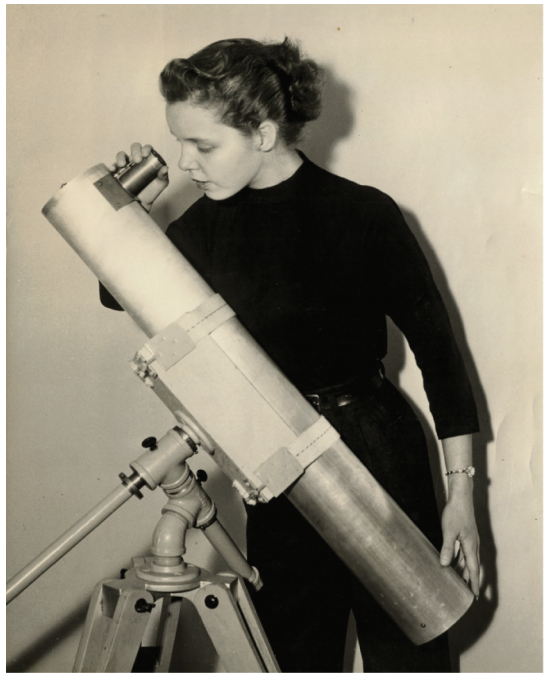

Figure 2
The author with T Ela Scope.

I saved enough money from my part-time sales clerk job to pay for aluminizing it (evaporating the mirror coating onto the surface) and having it professionally mounted. I christened it T Ela Scope (**Figure 2**).

"...AND WHY NOT TO"

In my final year of high school, I wanted to enter the Westinghouse Science Talent Search. There was an advanced chapter in my copy of Albert Ingalls's *Amateur Telescope Making* called "How to Make a Cassegrainian (and Why Not To)." That was an open dare. I could not resist it. Dr. Shatzel gave plenty of advice and encouragement. I completed the primary mirror and was well into figuring the small convex secondary mirror in time for Westinghouse entry. The project was every bit as challenging as the book had predicted. But I wrote it up, complete with challenges, and submitted it with my application form to the Westinghouse competition. That year I was one of 8 girls among the top 40 winners in the country who were invited to Washington, DC, for a week of exciting scientific events. My success in the national Westinghouse competition was the first evidence that, as predicted by that science aptitude test, I had unusual promise in science. But it had no impact on my choice of university. My father guided that decision. No, my father made that decision!

MY ALMA MATER, THE UNIVERSITY OF ILLINOIS

While my family was far from wealthy, we were by this time also far too prosperous to hope for university scholarship support. I received several honorary scholarships, including a National

Merit Scholarship, but they added up to only $100 per year. Even in 1956, that wouldn't make a dent in tuition at a private university. My father, keeper of the checkbook, announced firmly, "He who pays the piper calls the tune. I have paid taxes to the state of Illinois for years, and Illinois has a *fine* state university. You are going to the University of Illinois."

There was a certain clarifying simplicity to his view. And in hindsight, he was absolutely right. My oldest brother, Pete, back from army service in Korea, was in graduate school at the University of Illinois already. September came, and I was to ride in the back of Pete's car to my new home in a university dormitory. As I stepped out the front door, Pete told me to stop, turn around, and look back. He advised, "Say goodbye to this house. You do not live here anymore. From now on, you will be a guest in this house. Your childhood is over." My brother's words were eerily prophetic. By Thanksgiving, our Hinsdale house had been sold, and my parents had moved to Montreal, Quebec, following my father's latest promotion. We had lived in Hinsdale for less than five years. I felt homeless.

PROBLEMS WITH PHYSICS AND ASTRONOMY

I chose physics as my major, in view of my interest in optics, but I encountered a big problem: I fell asleep during the freshman physics lectures. That was probably the fault of my excellent high school physics class, which had already taught me most of what the college freshman physics class covered.

Although the University of Illinois did not offer an undergraduate major in astronomy, there were astronomy courses open to undergraduates. The requirements for the first astronomy class, according to the catalog, were "first year calculus and sophomore standing, or permission." Although only a freshman, I thought that I should be able to talk my way in. I approached the University of Illinois Observatory building at the appointed hour to be interviewed by Dr. Tull in room 101 Observatory. It turned out to be an unhappy interview: Tull denied my request to take his class, mainly, it seemed to me, because I was a freshman. I was valedictorian of one of the best high schools in the state. I had been in the calculus club, and had "proficiencied" out of the first semester of calculus and was signed up for the second one. I had made two telescopes, for heaven's sake! So Tull's argument that I needed calculus to understand astronomy, while presumably true, seemed a pretty lame excuse to refuse me admission. I was furious! I left and never came back. I never took a single astronomy course.

I AM A CHEMIST

Thus, uncaptivated by physics, unwelcomed by astronomy, I became a chemistry major. I loved organic chemistry. Before long I could ask questions to which we did not yet know the answers. I could sense what I thought of as "the edge"—the unknown. I stayed a chemistry major in what they called the Chemistry Curriculum for the remainder of my undergraduate studies, which were heavily weighted with technical classes and light on liberal arts. I spent much of my senior year doing thesis research on anthracene photodimers, beautiful bicyclic structures that formed from anthracene under the influence of solar radiation: brilliant sunshine! My thesis concerned the structure of photodimer derivatives that were quite insoluble. In order to analyze their structures, I needed to do nuclear magnetic resonance (NMR) spectroscopy. The NMR had to be run at a high temperature to achieve a high enough concentration of my compounds, but the solution must not boil. I finally thought of using a solid instead of a liquid as a solvent. I used naphthalene, which melted at a low enough temperature but boiled at a high enough temperature to serve as the solvent for NMR. My thesis project succeeded (1, 11). I got the structure.

NO, I AM A MOLECULAR BIOLOGIST!

I remained at the University of Illinois as a graduate student in chemistry. To fulfill the course requirements for a PhD in chemistry, I had to declare a minor. I viewed that as a nuisance, but I followed the rules. I chose microbiology. Toward that minor I had the very good fortune to sign up for a course called "The Chemical Basis of Biological Specificity," taught by several luminaries in the new field of molecular biology: Ben Hall, Sol Spiegelman, and Noboru Sueoka. They taught not only about the structure of DNA, but also how it was deduced. They taught not only how the genetic code works, but also how it had been translated. They taught how we know which end of a protein molecule is made first. They taught about the transfer of the cell's information from DNA to RNA to protein. I loved it! I was so deeply fascinated that I decided that this was the area of research that I wanted to pursue for my thesis. I changed my thesis advisor and began work with Ben Hall, the only one of my three favorite professors who was in the Department of Chemistry. This was important to me because this was the department in which I had passed my preliminary exams, a rite of passage that I would not want to repeat.

THE DEPARTMENT OF GENETICS

I was delighted when Ben Hall told me that he had accepted a new position as a professor of genetics at the University of Washington in Seattle. Working with him would entail moving across the country with his laboratory and two other students in the summer of 1963. Having completed my coursework and passed my prelims, I had no problem arranging to fulfill my PhD requirements *in absentia* from Illinois. Together with Hall's two other former chemistry students, I became an amateur geneticist. We received a total immersion in genetics and learned much about chromosomes, recombination, fruit flies, yeast, corn, mice, and even human genetics. I devoured this new subject matter.

A NEW PHD THESIS PROJECT

I was fascinated by bacterial transformation, the process by which certain kinds of bacteria can be coaxed to take up purified double-stranded DNA and use it to correct mistakes (mutations) in their own genome. While attempting to do something else, I discovered serendipitously that *Bacillus subtilis* transformation also works with single-stranded DNA (5, 9), even though a Harvard thesis (13) had shown that it did not. The explanation for this discrepancy turned out to be that I was adding a little ethylenediaminetetraacetic acid (EDTA), a chelating agent that bound magnesium ions. Initially, I worked with single-stranded DNA that was a mixture of its two strands, which I called "Watson" and "Crick." When I managed to separate the Watson strand from the Crick strand, I showed that each one was genetically active (4). This was not a surprising result, but the experiment was enabled by my new single-stranded DNA transformation technique.

MARRIAGE AND LIFE IN SEATTLE

In 1966 I married Dr. Scott Chilton, a natural products chemist who had been a PhD student at the University of Illinois two years ahead of me and was now on the faculty of the Department of Chemistry at the University of Washington. Scott studied the toxic substances of the poisonous orange mushrooms that grew abundantly in the Seattle area. Scott and I had many interests in common. We both loved working on our experiments in the laboratory. In addition, we loved hiking, backpacking, mountain climbing, and paddling our canoe. We explored natural

Figure 3

On a 1969 field trip with a freshman botany class from the University of Washington, my husband, Scott Chilton, assists me in photographing a wildflower, while our first son, Andrew, enjoys the activity.

things—mushrooms, wildflowers, rocks, and the inhabitants of the rain forest of Olympic National Park (see **Figure 3**). We especially loved hiking the Pacific coast strip of Olympic National Park and exploring Pacific tide pools, building driftwood fires, and collecting beach treasure.

One New Year's Eve, we snowshoed on a hiking trail and camped out at a three-sided trail shelter near Olympic Hot Springs in Olympic National Park. It snowed hard all night, and the snow was thigh deep by morning. We wallowed out to the Hot Springs Hotel at the trailhead, where we stayed until the electrical power was restored and the road was plowed. I remember Scott asking me (once we were in a warm, dry place), "Have you ever figured out what makes you want to do things like this?" It was a good question! We were not totally devoid of common sense; at least we never did it again.

We climbed Mount Olympus, Glacier Peak, Mount Baker, Mount Adams, and Mount St. Helen's (before the eruption that blew its top off). Scott, who was stronger and more adventurous than I, also climbed Mount Rainier several times, as well as some serious peaks in the Rockies. I learned to ski, one outdoor activity that Scott did not enjoy. I speculate that Scott, as a mountain climber, just did not like falling, an inevitable part of skiing. When our sons, Andrew and Mark, arrived, they became my ski companions at an early age. They didn't mind falling. They were good at it!

POSTDOCTORAL RESEARCH

By 1967 I had written my PhD thesis and traveled to the University of Illinois to defend it and pass my final exam. I was fortunate to be awarded a Public Health Service postdoctoral fellowship to work with Brian McCarthy in the Department of Microbiology and Immunology at the University of Washington. The central interest of McCarthy's laboratory was DNA. It was the best place in the country, perhaps in the world, to learn what was at the forefront of techniques for DNA manipulation at that time.

FILTER-BOUND DNA EXPERIMENTS

We made DNA filters (12) by denaturing DNA and letting the solution pass through cellulose nitrate membrane filter material to which it bound tightly. (Picture a smooth sheet of paper with little DNA strands bristling out from its surface like whiskers.) We pickled the membrane so that it could bind no more DNA. Then we baked it to make the DNA already bound stay put. Finally, we used a paper punch to excise identically sized little circles, each with the same huge number of DNA strands hanging off it. These little circles could now be incubated with radiolabeled single-stranded DNA at 65°C, and if the two DNAs were related, the hot DNA would bind to the filter-bound DNA, forming duplexes (still bristling off the little circle). We could measure the rate of binding by using a series of circles and removing, rinsing, and counting one at each time point. We could see how well the two DNAs matched by determining their melting profile, which involved heating a series of filters stepwise to higher and higher temperatures and counting the radioactive DNA remaining at each step. Duplexes that matched perfectly should have the same melting point as native DNA.

DNA filters are very versatile. The peril they pose is that the DNA used to prepare the DNA filter must be of high purity. Contaminating proteins or polysaccharides can adhere during DNA filter preparation, producing circles to which any labeled DNA, related or not, can bind.

C_0t CURVES

In another type of study, we measured the rate of renaturation of DNA in solution, i.e., the rate at which the Watson and Crick strands, once separated by denaturation, come back together in matching alignment to re-form the double helix. The rate of this process depends on the DNA concentration and sequence complexity. Viral DNA strands find partners much more swiftly than human DNA strands do, for example. The rate of renaturation can be measured by following the change in absorbance (or optical density) (OD_{260} mμ, the maximum for DNA) versus time. If the DNA is radiolabeled, one can pour a sample into a column that separates single- and double-stranded DNA. Either method gives a measure of the percentage of single-stranded DNA, and that value is plotted versus $\log_{10}$ of C_0t, where C_0 is the concentration of DNA and t is time. This plot, devised by Britten & Kohne (3), is called a C_0t curve. For simple DNA, such as bacterial or viral DNA, the value of C_0t at which the DNA is half renatured, $C_0t_{1/2}$, is proportional to the genome size of the source organism.

MISMATCH BETWEEN GENES OF DIFFERENT BACILLI

One of my postdoctoral projects exploited my *B. subtilis* transformation experience combined with the idea of the melting curve. I thought of a way to measure the melting point of individual bacterial genes. (Remember: This was before the discovery of recombinant DNA to separate individual genes.) I could heat the donor DNA to a series of higher and higher temperatures, testing the transforming activity for each gene of interest at each step. As the temperature of the transforming DNA reached the melting point of a particular gene, its strands would separate, and the transforming activity for that gene would decrease. (Of course, these assays had to be done under conditions where single-stranded DNA did not transform *B. subtilis*: no EDTA.) I later used this idea to measure the mismatch between a gene of one strain of *B. subtilis* and that of another, and even between a gene in two species of *Bacillus*. The genes that were more mismatched transformed my strain with much lower efficiency, if at all. Only the most conserved part of heterologous donor DNA could be transformed efficiently (10). I took to heart the lesson that transforming DNA needs

good homology to recipient DNA in order to recombine efficiently. While correct in this situation, this lesson would soon be challenged by new findings in higher organisms.

MY FIRST JOB

The arrival of our second son, Mark, in 1970 coincided with the end of my postdoctoral studies. After two months of being a stay-at-home mother, I was in a mood to take any job that would get me out of the house. Professor Helen Whiteley of the Department of Microbiology and Immunology at the University of Washington called me to ask whether I would teach the DNA methods laboratory course for her. It would be a temporary part-time instructorship, but it would be a job! I jumped at the chance. That turned out to be a very good decision. Not only did it get me out of the house—it brought me acquaintance with a student who knew the story of *Agrobacterium tumefaciens* and crown gall tumors. As a class assignment, Tom Currier presented a paper on crown gall DNA filter hybridization (14). Like me, my students were troubled by the paper's conclusion that *Agrobacterium* could insert a gene into a plant cell and thereby cause a plant cancer. To support such a claim, one should provide impeccable evidence. The authors had not done so. We noted several controls that had not been performed. Currier told me that his advisor, Professor Gene Nester, wanted to begin a study of this problem.

I approached Nester with a sales pitch: I knew exactly the right kind of DNA experiments needed to figure out what *Agrobacterium* was doing to these poor plants. In a nutshell, my idea was that I could measure the renaturation rate of labeled *Agrobacterium* DNA (probe) alone or in the presence of crown gall tumor DNA. If the tumor DNA had any copies of the bacterial DNA, the tumor DNA would in effect increase the concentration of *Agrobacterium* DNA, and the probe would renature more quickly. Nester was easily convinced. We asked Milt Gordon, a biochemistry professor who worked on tobacco mosaic virus, to join our project team because of his plant expertise. I wrote up a research proposal. We were awarded three years of research grant support, and most importantly, I had a job!

Currier ordered *Agrobacterium* cultures from the American Type Culture Collection. Gordon provided young tobacco plants, and Currier scrubbed their stems with alcohol to surface sterilize an area that he wounded and inoculated with the bacteria. After several weeks, we saw tumorous growths at the wound sites. After what seemed a long wait for the tumors to grow larger, we cultured them axenically, free from bacteria, by excising chunks of tumor, surface sterilizing them, and planting bits on plant tissue culture medium. A few succumbed to fungal or bacterial infection, but soon we had tumor lines that grew luxuriantly without added auxin or cytokinin, a defining property of crown gall tumors. We learned how to extract DNA from cultured tumors and began our studies.

I have summarized elsewhere the story of our *Agrobacterium* adventures in more scientific detail (6, 7) than we will need here. The first couple of years of our investigation seemed to be spent finding that the published evidence for DNA transfer to transformed plant tissue did not hold up to more detailed analysis. There were three reasons for this. First, the crown gall tumor DNA used to prepare the DNA filters was not sufficiently pure, and important controls that would have shown this were not performed. Second, the methods used (various kinds of DNA filter hybridization) were not sufficiently sensitive to detect the presence of a single copy of bacterial DNA per tumor cell. The third and most fundamental problem was that nobody was looking for the right DNA yet. Success had to await a discovery by Ivo Zaenen (17), a student of Marc Van Montagu and Jeff Schell at the University of Ghent in Belgium. Zaenen discovered that *Agrobacterium tumefaciens* contains giant plasmids big enough to encode 100 genes or more. Plasmids are circular DNA molecules that are not part of the chromosome. They contain genetic information that is not

normally required for survival but is useful in special circumstances. Zaenen found these while looking for something else, and it took a while to recognize the breakthrough. These huge and diverse plasmids conferred virulence on *Agrobacterium* (15, 16) and were therefore named tumor-inducing (Ti, pronounced "tee-eye") plasmids. Clearly, if DNA transfer were the cause of plant cells becoming tumorous, the Ti plasmid from the inciting strain would be the right kind of DNA to blame. In order to test for Ti plasmid DNA in tumor DNA, with high hearts we measured whether radiolabeled Ti plasmid DNA renatured faster in the presence of tumor DNA than it did by itself. The result was a clear no! We made reconstruction mixtures of normal tobacco leaf DNA with authentic Ti plasmids and showed that our method easily found one copy of plasmid per plant cell if we put it there.

At this point, we were disillusioned with the whole project. Some of us were ready to give up. But we decided to press on with one final attempt. Our earlier experiment would not have detected a small part of the plasmid if it were in the tumor DNA. We could separate the fragments of the Ti plasmid by gel electrophoresis and test them one by one to see whether any part of the plasmid was in the tumor DNA. This would be a huge experiment that would require the collaboration of our entire research group, working around the clock for about 60 hours. Timing was urgent because DNA labeled to the high specific activity needed for these measurements would be usable for only 60 hours or so before it would succumb to damage from its own radiation and become too small to hybridize. We all agreed to pitch in and dedicate a weekend to the project. We subsequently called this a brute-force experiment, for good reason. When our first experiment gave us a positive result, it amazed some of us and gratified others. We could scarcely believe our eyes. We didn't, not really, until we had repeated it. Our paper was published in 1977 (8). The plasmid DNA that we found in the tumor cells was named T-DNA (for "transferred DNA").

Each of us who participated in the brute-force experiments had the feeling during subsequent days of work that we were standing still. We had worked so hard and fast over the brute-force weekend that a normal day's work seemed like sleepwalking. As I have encountered my colleagues one by one since that time, we have reminisced about how we still cherish a spiritual aspect of that experience. Doing that experiment together created a unique bonding that we have sought to rediscover in our careers but never found again.

TIME TO GO

Success brought what should have been sufficient credit to Professors Nester and Gordon and me, yet along with it came friction. Usually a person of cheerful and optimistic disposition, I became unhappy. Perhaps strife was inevitable, given the circumstances. I see now, much more clearly than I did at the time, that the contributions of each of us, the mix of knowledge, skepticism, and belief that we had among us, were essential to our winning the race to find T-DNA in crown gall tumor DNA. We were all deserving of credit. Indeed, the credit I received would have launched my career, except for the small problem that I did not have a career. I was 38 years old with a soft money appointment and could find no opportunity for a tenure-track position at the University of Washington. The core of the problem was that, because of Scott's career, I had no geographic mobility. Nevertheless, it was time for me to go.

Scott knew me. He knew how I loved my work, and he saw that my situation had become untenable. He understood exactly what I needed to do. He encouraged me to see what I could find on the national job market, so I sent out applications. The Department of Biology of Washington University in St. Louis was really keen to attract both of us. They provided a chemistry laboratory for Scott in the biology building and appointed him a visiting faculty member. I became an

Figure 4

The author admiring a tobacco plant in the greenhouse at Washington University in St. Louis, circa 1982.

associate professor in the Department of Biology (see **Figure 4**). Scott was never a person who talked about his feelings, but the fact speaks for itself: He gave up his tenured appointment in Seattle and joined me at Washington University. Our family stayed together under one roof in St. Louis. Scott was a prince. Bless his heart. (He died in 2004 on a mountain-climbing trip on Mount Adams in Washington State, at age 70.)

A NEW LABORATORY AND AN OLD HOUSE

I loved the Department of Biology, and it loved me. Whatever I needed, everyone was eager to help. My colleagues offered the use of a scintillation counter, an autoclave, sterile solutions of antibiotics, and amino acids—anything I might need to get the laboratory up and running. I admit that it was a shock when I saw my new laboratories: They were completely empty, except for unopened boxes of incubators, water baths, pH meters, etc. On day one, my research group consisted of me and one work-study student. I was starting from scratch! Meanwhile, my competitors, including my former collaborators, were busily galloping on ahead of me. My reaction to this challenge was to seize a box cutter and get to work.

DOCTOR ERNIE

The world headquarters of Monsanto was nearby in St. Louis, and one of their research directors, Dr. Ernie Jaworski, took a keen interest in my work with *Agrobacterium*. Doctor Ernie was an early

visionary who would soon develop a research program at Monsanto on plant genetic engineering that would ultimately become the heart of the company's business. I was extremely fortunate that, immediately upon my arrival at Washington University, Doctor Ernie provided two postdoctoral fellowship stipends to help launch my program. All I had to do was write up a research proposal about what these postdocs would do. He subsequently hired me as a consultant. I had a new collaboration!

I was further aided by the arrival of Kotty Postle, a postdoc who had been working with me in Seattle. She had kindly agreed to come to St. Louis for a few months to complete her project, delaying her move to California. Technician Randy Saiki also came for a few weeks to help set up the laboratory. These bridging scientists stayed in the huge old house Scott and I had bought near the campus. In addition to setting up the laboratory, these young people helped out at home in the evening, putting up curtain rods and coaxing heat out of a crotchety old furnace. One of the hardships of the move was that we bought the St. Louis house many months before the Seattle house sold, and thus every penny of our savings was tied up in real estate. I still recall the embarrassment of asking my father for a loan so that we could buy a refrigerator, a debt repaid with my first paycheck from Washington University.

Over the next three years, my little group, by hard work, serendipity, and a collaboration with Professor Andrew Binns of the University of Pennsylvania in Philadelphia, managed to create the first genetically engineered plant and showed that the yeast gene that we had introduced was passed intact to its progeny. This success and that of our competitors (including the Monsanto group and the Schell and Van Montagu group in Belgium and Germany) were announced at the Miami Winter Symposium in January 1983. The birth of plant genetic engineering technology dates from that conference. A photograph of our genetically modified tobacco plant was published on the cover of the April 1983 issue of *Cell* that described our success (2).

MAY 1982: A VISIT FROM CIBA-GEIGY

During final exam week of 1982, three businessmen from a Swiss multinational company called CIBA-Geigy came to talk with me at Washington University. Their company was planning to establish an agricultural biotechnology laboratory in North Carolina, and they wanted to know whether I would be interested in being a candidate for the leadership of such a group. With Scott's encouragement, I agreed. One reason was that my aging parents lived in North Carolina and Scott's lived in Virginia. More importantly, this looked like a perfect opportunity to exploit the genetic engineering technology on which my postdocs had lavished so much basic research. It was time to plan for a way to put our new technology to work in the field. I was offered the position and joined the company in May 1983.

CIBA-GEIGY TO SYNGENTA

I had a lot of learning to do. I was good at recruitment, a very big part of the task initially, since we were starting from scratch. We leased a laboratory facility while building a new facility. I famously sketched for the architect on a paper napkin at the Raleigh-Durham airport what the layout of the laboratories and offices should be. The trees on our building site in Research Triangle Park became known as "Mary-Dell's trees," so fiercely did I protect them from our bulldozers. Developing the project portfolio had a lot of science involved. I had plenty to contribute there. But management in industry was new territory for me. It was interesting. I caught on. In the now 34 years since I moved to industry, this company (like many others in agriculture) has undergone mergers, spin-offs, and name changes. We are now called Syngenta. The years have included plenty of basic

research to learn how to work with real field crops. Tobacco was initially the white rat of the plant kingdom because of its ease of regeneration, but as the entire industry was to learn, it is a long way from tobacco to soybean, rice, sugar beet, wheat, cotton and hybrid corn! Each crop presented a whole new challenge. I learned that in industry, when an essential project isn't working, rather than adding more scientists to the team, you take some away. I learned, heart-wrenchingly, about saying goodbye, often to really excellent people. I learned that management can be very, very hard. After about a decade of administrative work, I jumped at an opportunity to return to laboratory work.

The technology of working with DNA had undergone so many changes that I needed retraining. A postdoc patiently helped me get up to speed again. There are now commercial kits for many procedures that were very challenging in an earlier era. Recent advances in technology for site-specific nucleases promise to increase the precision of genetic modification of crops. Genomes are said to be edited, so precise are the possible changes. This is indeed an exciting time to be involved in DNA research. I feel very fortunate that I am still able to be a participant.

EPILOGUE

While DNA technology is advancing at a heartening rate, we still confront the twin challenges of public perception of genetically modified organisms and the threat of global warming. Crop plants will be challenged. Plant breeders will need all of the technology we can provide. I am very pleased to be a part of the effort to address this need. If you are a student looking for an interesting and important career, we need you here. If you are a teacher, send us some bright minds. I cannot make any promises, but my career has been both challenging and enjoyable. It still is!

And now we have come to a good resting point. Perhaps, like me, you have lived long enough to notice that time flies faster and faster the older we get. In writing these autobiographical experiences, I found that same thing happening: The farther along in my life we moved, the faster I flew. A part of the reason for reading (and writing) any biography is to discover clues about what forces and events have shaped the individual that emerged. Those clues will likely be in the early part of life, if indeed there are any. There already exists a substantial published record of my scientific life (2, 6–8, and references therein); here, we have dwelt on my secret life. I hope you have enjoyed sharing with me this journey through my childhood and youth. I have enjoyed going back there, and you have been an engaging and agreeable companion. I thank you.

DISCLOSURE STATEMENT

The author is not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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