

LEE MARSHALL NADLER, MD: a conversation with the editor

Lee M. Nadler, MD, and William C. Roberts, MD

Lee M. Nadler (*Figure*) was born in the Bronx, New York City, on May 22, 1947. He was educated in New York City public schools. He graduated from Queens College of the City University of New York in 1969 and from Harvard Medical School in 1973. His internship and junior assistant residency were at Columbia-Presbyterian Hospital in New York City. In 1975, he went to Bethesda, Maryland, as a clinical associate in the Immunology Branch of the National Cancer Institute and after 2 years returned to Boston as a clinical fellow in medical oncology at the Dana-Farber Cancer Institute. At the same time, he was a clinical fellow in medicine at Harvard Medical School. Upon completing his training, he remained at the Dana-Farber Cancer Institute and rapidly rose in rank; by 1992, at age 45, he was a full professor of medicine. In 2002, he became the Virginia and D. K. Ludwig Professor of Medicine at Harvard Medical School and at the same time the Pan Mass Challenge Senior Investigator at Dana-Farber Cancer Institute.

Dr. Nadler's research in the 1980s focused on the discovery of molecules uniquely expressed on human B cells using the technique of monoclonal antibodies. He was the first to discover monoclonal antibodies directed against human B-cell-specific antigens and, in fact, all the known human B-cell-specific antigens (CD19, 20, 21, and 22) were discovered in his laboratory. He is a true translational investigator, since he used these monoclonal antibodies to classify human B-cell leukemia and lymphomas as well as to create therapeutic agents for patients. Today, every pathology laboratory in the world uses these discoveries in their pathology reports. More importantly, he was the first in the world to administer a monoclonal antibody to a human (a patient with B-cell lymphoma). His anti-B1 monoclonal antibody led to the discovery of the CD20 antigen, which led to the discovery of the therapeutic monoclonal antibody called Rituxan. Rituxan has changed the treatment of B-cell lymphoma; it not only impacts the lives of patients with B-cell lymphoma and leukemia but also is a major treatment

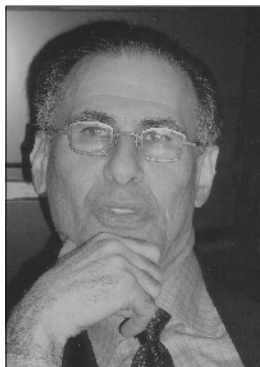


Figure. Dr. Lee Nadler during the interview.

for rheumatoid arthritis, systemic lupus, idiopathic thrombocytopenic purpura, and multiple sclerosis. Dr. Nadler also pioneered the use of monoclonal antibodies to “clean up the bone marrows” of patients undergoing autologous bone marrow transplantation for B-cell lymphoma. These pioneering studies opened the door to transplantation for patients with low-grade lymphoma and chronic lymphocytic leukemia.

By the 1990s, Dr. Nadler's laboratory and clinical focus had shifted to identification and characterization of costimulatory molecules on antigen-presenting cells and their T-cell counter-receptors. The most important discovery was the identification of the costimulatory molecule called B7. B7 is the critical signal that tells T cells to become functional or enter an inactive state called anergy or tolerance. B7 and its counter-receptors on T cells (CD28 and CTLA4) have become critical molecules for understanding the pathophysiology and drug development for autoimmunity and tumor immunity. In these arenas, Dr. Nadler has again demonstrated that he is a translational pioneer, and his work is now making breakthroughs in the fields of haploidentical stem cell transplantation and tumor immunity.

His work has led to the publication of >300 articles in peer-reviewed medical journals and to >100 reviews and book chapters. He has received a number of honors for his work. He is the proud parent of three successful offspring, one of whom, Eric, is an oncologist at Baylor University Medical Center (BUMC). Dr. Nadler is a very interesting fellow, and it was a pleasure having the opportunity to meet with him. Marvin Stone was instrumental in getting us together.

William Clifford Roberts, MD (hereafter, Roberts): *Dr. Nadler, I appreciate your coming to BUMC at the invitation of Dr. Marvin Stone. Thank you for the opportunity to talk to you and for the readers of BUMC Proceedings to get to know you. To begin, could you talk about your upbringing, some of your early memories, your mother and father, and your siblings?*

Lee Marshall Nadler, MD (hereafter, Nadler): I had a somewhat strange and difficult upbringing. I was born in the

From Dana-Farber/Harvard Cancer Center, Boston, Massachusetts (Nadler) and the Baylor Heart and Vascular Institute, Dallas, Texas (Roberts).

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Bronx, New York, in a relatively poor neighborhood, and my parents were pioneers, moving to Queens when it was still a forest. My parents were married by their 21st birthdays. My dad was very bright but had a troubled life. He told me that he attended City College of New York and played on the football team and that he was a Phi Beta Kappa. Later, I learned from my grandmother that he had never gone to college; he had bought the Phi Beta Kappa pin in a pawnshop and made up the entire story. What was more extraordinary was that he was able to educate himself sufficiently to be able to function as an electrical engineer without any training. Pretending that he had advanced degrees worked for him until the top-secret firms that he was employed by discovered that his records were falsified. By the time my dad was 50, he hardly ever worked, and that made our family life very difficult.

Mom was a stay-at-home parent. My maternal grandfather was a tailor, a hardworking man who had sent his son to dental school. My maternal grandfather provided a lot of our living expenses and served as a role model for me. Of the members of my family, he stands out, and his core values were the ones that I learned to embrace.

We lived in a small home in Queens. We didn't have much money, but to be honest I did not know it. I'm not actually sure how we lived through everything with my father's stormy working history. I was a moderately bright kid but not extraordinary. My high school record was probably good enough for me to attend a private college, but that was not in the cards. My parents sat me down and told me that the only way that I could attend college was to live at home and go to the local city college. In many ways, I was like the first-generation Americans who went to the City University of New York. It cost just \$34 a semester, and therefore my entire college education cost less than an application to an Ivy League school today. During college, I had to live at home for the entire 4 years with my dad at home nearly all of the time.

From my senior year in high school and all through college, I had a girlfriend who later became my wife. Her name was Ellen Soffer. Her family was much more of a rock to me than my own family. Her dad was a Holocaust survivor. As a 14-year-old Jew, he lived in Vienna, Austria, during the time of Hitler, and he and his 15-year-old brother got out. They traveled to Paris and then New York alone while their parents remained behind. He was a very concrete kind of guy. When he arrived in America, he made it to the lower east side of New York. As a young man, he swept floors and then sold women's lingerie as a salesman. He was an American soldier and spent most of the war behind German lines as a spy. Ellen had a very strong family upbringing, so I often hung out in her home. To say that I was a hungry kid who didn't feel very well grounded is an understatement, especially when I realize that I was really a kid who didn't have very much. My memories are of what I didn't have, not what I had. That is not to say that my family life was devoid of love, but there was lots of trauma in that family. My brother and I both describe ourselves as people who escaped.

I went to Queens College. My brother, who is 2 years younger than me, convinced my parents to send him to a state

university, and he chose Stony Brook. I do not know where the money came from, since it cost a few thousand dollars per year. He had always wanted to be an English teacher and thought little of my intentions to become a doctor. No one before me had ever made it from Queens College to Harvard Medical School. Queen's College opened in the 1930s, and I was there in the mid to late 1960s. I was so passionate about trying to become somebody different that I was really possessed.

The neighborhood I grew up in was very blue-collar. We all spent more time stealing than studying and reading books. About the time I figured out that my family was less well off and "different" and I wasn't going to have much, all I had ever read were comic books. How strange: I could not read, and I was already 14 years old. I realized that the only way I was going to be anybody better than the people who worked as blue-collar workers was to become better educated.

One summer day, I went to the library and said to the librarian, "I need a book." She stared at me. I said, "I need a book." She stared at me more. "No, please help me, I need a book." "What are you going to do with it?" she said. "I gotta learn how to read." Before that, I do not remember ever sitting alone and just reading a book. She brought me Pearl Buck's *The Good Earth*, a very small book that I read with my fingers under the words. It took me about 7 days to read its 150 pages. I went back to the same librarian, brought back the book, and asked for another one. Within about 3 years I had read Dostoevsky's *Crime and Punishment*, *The Brothers Karamazov*, and *The Idiot*. I was capable of reading major literature continuously by the time I met my girlfriend. I was determined to read the great books that had shaped history.

Roberts: *How many books do you think you read from the age of 14 until you went off to college?*

Nadler: By the time of my senior year, I was reading a serious book every week or two. Just after my 16th birthday, I read *Arrowsmith* by Sinclair Lewis. Martin Arrowsmith was a young physician, and I immediately fell in love with his character. He worked in the McGurk Research Institute, and his mentor was Max Gottlieb. When I finished the book, I knew when I grew up I wanted to be Martin Arrowsmith. I had never had the chance to speak with a physician or researcher, and so Martin Arrowsmith became my ideal role model. How frightening that I decided I wanted to be this book character. This book had an enormous impact on me. Sinclair Lewis was the first American to win a Nobel Prize in literature, and he won it for *Arrowsmith*. Sinclair Lewis was America's greatest writer of the 1930s, and his works include *Main Street*, *Babbitt*, and *Elmer Gantry*. I believe that *Arrowsmith* is one of the great books of American literature.

From that fateful day on, I knew who I wanted to be, what I wanted to be, and the person I wanted to be. In the last scene of *Arrowsmith*, Terry Wickett and Martin Arrowsmith are sitting in a boat talking about their research. My friend, Curt Civin, chairman of pediatric oncology at the Johns Hopkins Medical School, and I sat in a boat in the summer of 1977 and played that identical scene. We talked about the discovery of monoclonal antibodies and how they might change medicine. We were

both at the National Institutes of Health (NIH) together, and we were old friends. I felt like I was in *Arrowsmith* again, and who could have predicted how important that rowboat meeting was for the remainder of my life?

I knew college would be my route to another position in the world. I knew that it was not a time to party or simply to get good grades to get into medical school. It was my time to transform myself into a different person. Unfortunately, I attended a college that didn't get many of its students into medical school. It had 10,000 entering students every year; about 100 of them remained after 4 years to apply to medical school, and about 50 got in—not very good odds. Like most other students, I had to make the cut. The premed students had to take chemistry before biology, and if you didn't get a reasonable grade, you were no longer a premed major. Even when I got A's, I realized that from Queens College that would not be enough to distinguish me. So I tried to be different.

By the time other students were ready to take organic chemistry and its lab courses, I had found Albert Harold Blatt, PhD, chairman of the department of chemistry, who let me do research with him. When I met him, he was probably in his late 60s. He was an internationally distinguished man who had a PhD from Harvard, and he had even written the first organic chemistry book with the president of Harvard, James Conant (Conant and Blatt). He was the editor in chief of two journals: *Organic Reactions* and *Organic Synthesis*. After much persistence and begging on my part, he let me work in his lab. He didn't have graduate students, and I was probably the only college sophomore who had ever worked in his laboratory. I spent morning till night trying to understand organic chemistry in a laboratory as an undergraduate, being mentored by somebody who was extraordinary. Although I didn't publish anything, I had several abstracts in *Organic Reactions*. I was inventing things when other kids were going to the lab to do their coursework. Professor Blatt was my Max Gottlieb.

Roberts: *How did you find him?*

Nadler: Martin Arrowsmith had found a mentor who was the extraordinary person at his university, so I guess I looked for someone who I thought embodied the principles of Max Gottlieb. Blatt never spent much time talking to me about being a physician, but he kept telling me I could push harder and go to the next level. I think that was what Gottlieb did for Martin. I was always looking for some way to distinguish myself, so I became the editor of the *Queens College Science Journal*. Similarly, I tried to diversify, and therefore I was selected as a member of the student court and rose to the rank of chief justice. What a strange time to be the chief justice of the student court, when the first student sit-ins and racial tensions began to plague college campuses. Many times in this role, I was challenged to do the right thing even though I knew that the college administration might punish me.

Once again I was given an extraordinary leadership opportunity as an undergraduate. I had the privilege of sitting with the chancellor of the university on a program called SEEK (Search for Higher Education and Knowledge), which was for the entire City University of New York (>100,000 students).

The goal of this program was to create virtually open enrollment for any minority student who could graduate from high school and meet the admission standards of either the senior or junior colleges. What an experience: I found myself invited to meetings where undergraduates were usually not permitted. This experience convinced me that I had the determination and courage to take on hard tasks and to stand up for my principles. Comparing myself to the other students at Queens College, I am not sure very many were ever so diverse. I don't think there was a minute, 24 hours a day, 7 days a week, that I wasn't trying to figure out how to get to the next step. I epitomized the term *driven*.

Roberts: *Queens was a part of the City University of New York system? How many colleges were there?*

Nadler: Many. There were the City College in Manhattan, the oldest, which Jonas Salk attended; Brooklyn College; Hunter College (both in the Bronx and Manhattan); J. Jay Criminal College; and of course Queens College. There were about 15 junior colleges, such as Queens Borough Community College, with a massive number of students. The City University of New York was a brilliant concept. If you were good enough to go to college, cost would not prevent you from attending. Even though the college was free, I tried to work whenever I could. During college, when everybody else was on vacation in Florida or the Bahamas, I was working as a clerk registering students for the next semester or working in Blatt's laboratory. Once I blew up the laboratory during the weekend. No one was hurt, but the lab was a big mess.

Roberts: *You took the bus to college?*

Nadler: Yes, for the first couple of years. It was about 6 or 7 miles each way. I would go to college by 7:00 AM and come home when the library closed. By my junior year, I had an old, beat-up car, and this made coming and going so much easier.

Roberts: *During college, did you live in the home that you grew up in?*

Nadler: Yes. My mother still lives in the same house on 202nd Street. On March 3, my mother was 85 years old, and we moved into that house more than 50 years ago. Many of the rooms seem to be untouched since my brother and I moved out more than 30 years ago.

Roberts: *What was your house like?*

Nadler: It was a tract house that was built on plots of 40 × 100 feet. It was a small Cape Cod structure, which cost <\$10,000 when my parents bought it. My brother and I always shared a room. There were many troubled parts of our lives that bound my brother and me together. Our house was furnished by hand-me-down furniture from grandparents. That's how we grew up. I didn't have a desk, just a board on supports. We had plenty of food, but we didn't go on many vacations. Once we went to Washington, DC, another time to Philadelphia, and once to Canada. That was our childhood. We didn't go to summer camp. Looking back, it really was not so bad, but compared to the lives of my colleagues who traveled the world, I had a very restricted upbringing.

Roberts: *What did you do during your summers?*

Nadler: I did whatever I could. When I was young we played in the streets. We hung out with friends on street corners. The worst job I ever had was when I was 17, and that job convinced me that I must break out of that neighborhood. It was at R. R. Bowker Publishing Company in Times Square. I had to get up at 5:00 AM, take a bus and two trains to the 42nd Street area, and go into a small room. I typed envelopes from 7:00 AM to 8:00 PM every day for \$1.25 per hour. I felt like I was Rumpelstiltskin. Envelopes were piled from floor to ceiling, and I typed for 12 hours a day. No one ever spoke to me—not one word during the entire 14 weeks. I typed like a slave from morning to night. I was a good typist on one of those old IBM typewriters. I probably typed 1000 envelopes every day. By the end of that time, I decided that I was clearly going to do something else with my life. What was most difficult for me was that no one respected or cared about me.

Roberts: *Both your mother and your father were born in the USA?*

Nadler: Yes. They are both Americans.

Roberts: *Where were your grandparents from?*

Nadler: They came from Eastern Europe, although I do not know the names of the towns, and were driven to America by the prejudice that Jews faced there. The name Nadler means tailor in German. My ancestors in America were in the garment districts; they were laborers, and no one owned a big business.

Roberts: *Why did your father lie about his background?*

Nadler: Because he had severe psychological problems, and it was his only way of rationalizing and making himself feel respected. He would call himself Dr. Bernard Nadler and walk around with books, and it was all a fake. My childhood was very traumatic in the sense that I wanted out. Most kids love their families and want to remain at home. I wanted out as fast as I could. I wanted to run away. Maybe the best thing that ever happened to me was being forced to live there from the age of 18 to 22 because it turned me into a rock. There was nothing more you could do to me to knock me down.

Roberts: *Your father didn't work after the age of 50?*

Nadler: Correct. If he did, it was only intermittently. He was a television repairman when we were young. He would put antennas on tops of houses. One day the police came and told us that he had fallen off a ladder; he had a broken femur, and they had taken him to the emergency room. I remember that day very well. Thereafter, he worked a few months here and there and a few months in engineering jobs, but there came a point when he never worked again and was home all the time.

Roberts: *Your mother didn't work outside the home?*

Nadler: After my dad stopped working, she became a secretary. She had been a secretary when they got married.

Roberts: *When was your father born?*

Nadler: He was born in 1921 and died in 1986 at age 65 of metastatic prostate cancer.

Roberts: *What was your mother's name, and when was she born?*

Nadler: Miriam Rose Nadler. She was born in 1922.

Roberts: *It sounds like there was a great deal of tension in the home.*

Nadler: To be totally honest, while it was going on, I didn't know as much as you might think. Children don't see clearly. I lived in a neighborhood where there were lots of complicated families. I was always on the streets and out of the house. Not until my later teenage years did I realize there was a problem. I knew that things weren't simple. When I was in the Cub Scouts my father wanted to be the scoutmaster, and he was bizarre. He had to wear the headdress. He was a very strange guy. One year he insisted on building my science project for school and carrying it into school himself. I was very embarrassed. I told the teacher that I didn't do it and to flunk me.

Roberts: *Did you eat dinner together at home at night?*

Nadler: More often than not.

Roberts: *Was there any conversation around the dinner table?*

Nadler: Television was on right next to the table.

Roberts: *Were there any books around the house?*

Nadler: Sure, old books and "Book of the Month Club" books. My grandmother's brother had left some books; they are still on the same shelves after 50 years. There were engineering books and old engineering journals from my father. My brother and I bought some hardcover and paperback books.

Roberts: *Did your mother or father read?*

Nadler: Not very frequently; at least that is what I remember.

Roberts: *Did you take a newspaper?*

Nadler: Yes, one of the New York daily newspapers. I don't remember seeing a *New York Times* very often.

Roberts: *When you came home with a report card from school, did your parents say anything to you? Did you show it to them?*

Nadler: I always had to get them to sign it. I always did fine. I was in the upper middle of the class, and I don't think I gave them anything to be embarrassed about.

Roberts: *Did you have any teachers when you were in elementary through high school who had an impact on you?*

Nadler: Not really.

Roberts: *Was your mother warm? How did your mother and father get along?*

Nadler: My father was verbally abusive. Mom was warm, or at least I remember her being kind and caring toward Paul and me. My mother simply cared about her children. Sometimes when I would watch the TV show *All in the Family*, I thought I lived in that house and that my mom was Edith Bunker. That's how my dad treated my mother.

Roberts: *What about your brother?*

Nadler: I strongly believe that human beings become who they are by either emulating or rebelling against their families. My brother, Paul Ira Nadler, was rebellious like I was. Paul was the brighter of the two of us. He was always going to be an English professor. I think that he was so moved that his older and much less talented brother was admitted to Harvard Medical School from Queens College that he transferred to Queens College from Stony Brook to try to follow in my footsteps. He went right to work when he got to Queens. When I graduated, I won the Jonas Salk scholarship, a 4-year scholarship to medical

school awarded to only a few premedical students of the entire City University. Paul also won the Jonas Salk scholarship.

Roberts: *That was the whole City University of New York, including all boroughs?*

Nadler: Correct. There is a group called the Society of Salk Scholars, about 100 total people over 35 years. Paul didn't get into Harvard, but he got into Washington University Medical School in St. Louis, and he trained at Barnes Hospital. He was one of their stars. My brother got married when he started medical school just like I did, and Paul then finished his housestaff training and went to NIH to work in the same lab with the same person I did.

Roberts: *Who was that?*

Nadler: Dr. Richard Hodes, now the director of the Institute of Aging. I was Hodes' first postdoctoral fellow. My brother was probably his third or fourth. Hodes had gone to Harvard Medical School. When Paul was at the NIH and I was already an assistant professor at Dana-Farber Cancer Institute, Paul came up to interview for an oncology fellowship. He was a shoo-in. When he was about to leave, he told his interviewers that he was not impressed by Dana-Farber. They wanted to accept him, and he turned them down and went into industry. My brother is now one of the most prominent regulatory consultants in oncology in the USA.

We were quite competitive. When I was a fourth-year Harvard medical student in 1973, I had a son, who now works here at BUMC—Eric Nadler. Six months later, Paul had a son. My father was one of three brothers, and his father was one of three brothers, so on the Nadler side there had never been a daughter. When I was at NIH in 1976, my wife was pregnant. At the same time, my brother's wife was pregnant. My daughter was born and of course his daughter was born, and then we each had another daughter in sequence. In his first family (he's remarried), he had a son and two daughters; I had a son and two daughters. If you define sibling rivalry, Paul and I are the epitome.

Roberts: *You look like a pretty strong guy. Were you an athlete?*

Nadler: When I was in high school, I ran track and cross-country. I ran an average mile. If I had been at a better school with a track coach, I might have been quite good. I got a bad injury to one Achilles tendon when I was a junior in high school. In my 30s, I ran marathons. Today, I work out all the time, and I believe that I am in better shape now than at any other time in my life.

Roberts: *How did you get interested in science? Entirely through Arrowsmith?*

Nadler: Yes.

Roberts: *Had you taken a science course before that in high school?*

Nadler: Sure. Every kid did in New York. It was required. I also liked history. I was terrible in language and fair in math. I was not a good writer, but I was a good reader. I've become a good writer subsequently.

Roberts: *Did you do crossword puzzles? Have you ever done them?*

Nadler: No. Before taking the SAT in high school, I bought Barron's test preparation book, which contained 2500 words, and I memorized all 2500 of them. Then, I got another book and memorized 2500 of those words. I got all the words correct on the SAT. When I say I had a passion to "get the hell out of Bayside," I meant it. I went through every single word in those books, underlined every word, and looked them all up.

Roberts: *You never needed more than 4 or 5 hours of sleep? Is that right?*

Nadler: No, I am always tired. I work hard. Five to 6 hours of sleep is great. When I was a houseofficer, I hardly remember sleeping at all every other night and then every third night.

Roberts: *When you were at Queens College, I presume your chemistry professor advised you to go to Harvard Medical School?*

Nadler: No. As a matter of fact, he never even commented. He was very much like Max Gottlieb in *Arrowsmith*, a little bit like I treat my own son. He left me alone. But he did tell me that I was special and that I was different. That is all you need to tell somebody. You don't need to say another word. You can say, "I haven't seen anybody like you." The premedical advisor at the college was Daniel Marien, and he did not care for me. I was a chemistry major and not a biology major, and he expected students to brownnose him. That wasn't and never has been my thing. He decided that he would push for three of my classmates at Queens for admission to Harvard Medical School. Of course, I wasn't one of them. I remember that one was a woman biology major named Regina. He liked her because she played the cello. Marien also liked a friend of mine named Arthur Reba, who had nearly perfect grades. Marien pushed for them, and Harvard interviewed all three. Before I had even been offered an interview, these three students were told they were going to get a second interview in mid-January at the Waldorf-Astoria Hotel in New York City.

Sometime in late November, I got a letter inviting me for an interview at Harvard in Boston. I remember the day I went, the day that everyone left for Christmas vacation. I was 21 years old and had never been on an airplane. I had about \$250 in the bank from my regent scholarship, and I took it all because my parents didn't have anything to give me. I had an old blue suit, and I borrowed an overcoat since I didn't have a nice winter coat. A surgeon interviewed me first in the Harvard Medical School complex, and I was told that later in the afternoon my second interview would be at the Massachusetts General Hospital (MGH) across town. I asked if someone could show me around. I was told that no one was available but that I could walk around. I did. Then it started to sleet and snow, and I was told to take the subway, which is above ground. After three attempts at trying to get subway directions to the MGH, I started walking the 3 miles.

When I got to the Warren Building of MGH, I was sopping wet. I made my way down to the pathology suite, where Sanford Roth was going to interview me. My teeth were chattering. This was 1968. The Vietnam War was raging. In his office, Dr. Roth had a map of Vietnam with boats and planes all over the map. I felt like I was in a Fellini movie. I was shivering, had spent all my money, and thought that Harvard was not going to take me

anyway. Dr. Roth looked at me and said, "Great war. I'm really excited about it." I smiled and said, "You are?" I told him that I didn't agree with him. We started talking about it. We argued about it. I looked at him and said, "I just spent my last nickel, and I'm freezing my tail off. You didn't ask me anything about myself and I'm not getting in here, so why are we doing this?" He looked me straight in the face and asked if I was cold. I said, "Yes." He said, "Let's get you some scrubs and dry that suit." He gave me a set of scrubs. I stripped down to my underwear, and he put my clothes in one of those pathology dryers. He asked me how many kids I thought came through this office and fought with him. I told him I didn't know. He said, "None. You are an interesting kid." We continued talking for another hour. He said, "The likelihood of your getting in here is zero, but I'm going to fight for you." He drove me to the airport, and I went home and told my fiancée that I didn't know what had happened but I thought I was going to get a second interview, which was scheduled for January 15.

On January 10, I was sitting upstairs with my girlfriend at my parents' house when the doorbell rang. My father screamed up the stairs that I had a telegram from Boston. I went on like a motor mouth for an hour that the telegram probably was inviting me for a second interview. I didn't even go downstairs. About 11:00 PM, I went downstairs, got the telegram, walked upstairs, and opened it. It said, "Pleased to announce your acceptance to Harvard Medical School class of 73, Perry J. Culver." My first words were that it must be a fake. I thought one of the guys from Queens College now in Boston at medical school had sent it as a joke. I'm mouthing off for the next hour about it being a fake, and my fiancée advised that I find out. She said, "Call Western Union and find out where the telegram came from." I called Western Union and read them the numbers on the telegram and they said it came from Harvard University teletype. I sat down and wondered how it happened. What did I do that got me out of here, because I'm outta here! On that exact moment on January 10, 1969, I was out.

Roberts: *Did you go by and see Dr. Roth when you were at medical school?*

Nadler: No. I didn't say a word to him. I didn't know much what to think about it. I was so scared.

Roberts: *Did you have a scholarship to Harvard?*

Nadler: I had the most amazing scholarship. We were poor by Harvard standards, and I filled out the appropriate forms. My Jonas Salk scholarship was for \$3500: \$875 a year for 4 years, and my Harvard tuition was only \$2500 a year. Harvard gave me a scholarship for about \$1000 per year. The medical school gave me loans, and at the end of medical school I had only \$5000 worth of loans. My son was born 5 weeks premature, and I had to go ask the dean if I could borrow \$2000 to cover living expenses since my wife had planned to work until March.

I would argue that very rarely does such a complete turnaround happen. Here I was a kid who basically thought I was never going to make it to the next step. I was positive that I would get into some medical school, but I didn't want to go to downstate, which was par for the course at Queens College. I was hoping that I might get into Einstein or New York Univer-

sity. By early in the fall of the application process, I knew that I was going to do better because the University of Pennsylvania interviewed me on a Saturday in early September, and I was accepted a few weeks later.

Roberts: *You had that in your pocket before you went to Harvard?*

Nadler: I had several in my pocket by the time I went to Harvard for an interview. I don't remember all of them. I had a feeling that New York University was going to turn me down. Dorothea Franklin hated me at the interview, and Columbia rejected me without an interview. Later, when Columbia offered me the position of chairman of oncology, I rejected the offer without an interview. I told them turnaround was fair play.

Roberts: *You had never lived away from New York or your family's home. Now Boston? How did it go?*

Nadler: I got married on December 21, 1969, three months into medical school.

Roberts: *You got into medical school before you got married. What was it like initially in Boston? The intellectual people you were now with must have gone up a notch or two.*

Nadler: The first day I went to Harvard Medical School, I wore a three-piece suit. It was the first nice suit that I ever owned. Everyone else showed up in jeans. I was the hick from New York and Queens College. There were 140 students in the class at Harvard Medical School, 110 of whom had gone to Ivy League schools. I lived in the dorm for the first 3 months even though I had already gotten an apartment for our upcoming marriage in December. I wanted to experience the dormitory life since I had never done so in college.

One Friday night, Joseph Collins Corkery, now a friend for 35 years, was going to bring his girlfriend back to his room. In Vanderbilt Hall, they had fireplaces in one or two of the rooms on each hall. I wanted to be a real buddy and went into his room and built him a fire. Unfortunately, I didn't know what a flue was. When he got back to the dormitory, the entire Vanderbilt Hall was surrounded by fire engines. I had filled the entire place with smoke. Not only did Joe not get the girl to his room, he didn't ever get her into the building!

One guy in my class, John Guyton from Mississippi, hung rattlesnake skins on his wall the first day in the dormitory. His father, Arthur Guyton, was one of the great physiologists of all time. In fact, John had attended Ole Miss for free since his father was a professor there. John was part of a Harvard dynasty. John and all of his seven siblings would eventually attend Harvard Medical School. I was beginning to figure out how things worked at Harvard.

Although my passion and drive didn't let down, I had a much harder time navigating than I had at Queens. I did not understand this giant complex, and it took me a very long time to ramp up to understand Harvard. During my first year at medical school, I was positive I was going to be a surgeon. That's what I wanted to be, but I had no idea why.

Roberts: *This was before you were on the wards?*

Nadler: Yes, and also when I was on the wards. I went right up to 3 days before match day before changing from surgery to internal medicine for internship. I went to the dean and said

that I wanted to go into internal medicine. My son had been born and I wanted to go back to New York. I placed Columbia first, and that's where I went.

As a senior in medical school, I had an experience that was as difficult as my interaction with my father, and it actually affected who I am today. A good friend and classmate, David Keith Lee, who lived across the hall and was from Lead, South Dakota, and I decided to do research together as senior medical students. We did this without a mentor, since we couldn't find one. Stanley Order, who had published an article in *The New England Journal of Medicine* with Samuel Hellman (Sam was the great radiation therapist of Boston), had some Hodgkin's disease tissue. David Lee and I wanted to figure out, by ourselves, what the immune defect was in Hodgkin's disease. Drs. Order and Hellman gave us laboratory space but nothing else. We bled each other every day. We borrowed other faculty members' laboratory equipment, and we isolated a factor from the spleens of Hodgkin's disease patients that suppressed the ability of lymphocytes to become activated. This was 1972. We used columns and did chromatography. I think that we must have discovered tissue necrosis factor!

We wrote it up and planned to publish it. I was so excited about our discovery. Then I went to defend my honor's thesis at Harvard Medical School. In the room sat David Katz, who was a protégé of Baruj Benacerraf, 1980 Nobel laureate in medicine. Katz took us apart. I had a gray suit on, and when the thesis defense was over, there wasn't an inch of that suit that was dry. He tore us apart for no reason. Katz was a hated man, and he deserved it.

Roberts: *What department was he in?*

Nadler: Pathology.

Roberts: *Why was he so belligerent?*

Nadler: That's just the way he is. Years later someone tried to poison him and failed. Katz didn't like what David and I had done, and instead of encouraging us, he tore us apart. He quizzed me on a paper by Dick Gershon from Yale. Gershon had discovered something called "suppressor cells." David and I thought they were important, and I later worked on them at the NIH with Hodes. They went out of favor until a few years ago, and of course today they are again a centerpiece of all the problems of autoimmunity and immunotherapy. Katz told me that I was an idiot and had no taste. I walked out of that honor's thesis defense and said to my wife, "Forget it. I'm out of here. That's the end of my research." I had worked day and night, 10 hours a day for 10 months, and somebody basically told me that I was an idiot. I was so mad and insulted that I did not go to my medical school graduation ceremonies. I got into my car and went to New York as soon as the last lecture was over. I swore I would never, ever do research again. I thought that Katz and his colleagues were crazy and I would be insane to stay in Boston.

Roberts: *What were the features of your future wife that attracted you to her?*

Nadler: Ellen and I were divorced 5 years ago. She and her family were everything that my family was not. They were concrete. She was pretty, nice, and believed in me. I think we

had similar values at that time. I met her mother when I was 17, and she said to me at that time that "I was 17 going on 40." And I was. For Ellen, my life was planned out. I got engaged at 19 and married just before my 22nd birthday, and my son was born before I was 26. I had three children by my 31st birthday. I had a master plan written out. As much as my father and my family wandered, I was focused.

Roberts: *You were at Columbia how long?*

Nadler: Two years. I short-tracked. It was wonderful. There were wonderful physicians on the medical service. Harvard was not built on great clinicians. Columbia was built on the ethics of medicine and on a great medical service. I loved being a doctor there and prided myself on being there. My patients came before anything else. I learned a lot about medicine. Some of the private patients I had an opportunity to take care of included Charles Lindbergh, Duke Ellington, and the Aga Khan, who told me he got weighed in gold each year. My first medical student was Jerry Groopman, who writes for the *New Yorker*. I had medical students who were extraordinary. There was a tradition, a history, at Columbia, just like other places. It is a great medical institution.

What made me go to the NIH? Within a year from the time of that bad episode of research at Harvard, I decided that I would give it another try and go to the NIH. I joined a group of immunologists. We worked on mouse immunology. I couldn't see where the mouse was going to lead me. In my mind, I gave NIH a C+ and headed north.

Roberts: *You were at NIH for 2 years?*

Nadler: Yes. I was pretty sure that I was going to finish at Columbia and then go to Dana-Farber for a year or two, finish up there, and head right to Park Avenue in New York City. One prominent oncologist at Columbia, George Hyman, told me that I could drive a Rolls Royce someday. But there was something missing inside of me because every time I tried to head in the right direction to Park Avenue, I make a left turn. I went to Dana-Farber to do a clinical fellowship. It was not a great place to train in clinical medicine. For as great as Columbia was, Dana-Farber was different. The patients were great! Learning how to be a cancer doctor was great.

I then decided that I wanted to take one more chance at research. I was at the right place at the right time. I was advised not to work with the person I worked with, Stuart Schlossman. I was told that he was a really tough guy and would treat me poorly. I walked into his lab with an idea about monoclonal antibodies and human disease. He said no and told me to get a rabbit. I worked on rabbits for 3 months. I then walked back into his office and said I was not working anymore on rabbits. He told me that no lab investigator had made a monoclonal antibody and that I would have to wait for a company to make one. I said, "Like hell." I found a former classmate of mine, Phil Stashenko, who had gone to Harvard Dental School. Phil had a PhD in immunology. He was trying to make monoclonal antibodies against strep mutants, i.e., tooth bacteria, put the antibodies in mouthwash, and make a billion. It was a great idea, but he had had no success.

We teamed up and worked brilliantly together. I told him that I wanted to cure non-Hodgkin's lymphoma, and the rest is history. Basically, everything we touched worked. I can summarize a lot of my academic career as a series of grand accidents. We asked the right questions. My mentor didn't mentor me at all; in many ways, he had some of the traits of my father. He was a very abusive guy when I was in his lab.

Roberts: *You remind me of Gary Player, the great golfer, who said, "You know it's a funny thing, the more I practice the luckier I get."*

Nadler: He's right. Here the environment might not have been good, but it was a perfect moment. My boss told me that my work was garbage when we discovered the B-1 antibody; he said it wasn't important because he was working on T cells. I didn't believe him. Now, as I look back, he did provide a very good environment, and he was just the expert on tough love. We are friends now. He is now 72 years old. When he was 50 years old, he made a career change. He kept his office but he stopped doing active research. He wanted to be the president of the institute or the winner of a Nobel Prize. He deserved both. Now I look back on this guy, and I have decided that he was extraordinary.

Roberts: *It sounds like you always have been independent. You got out of your house because you didn't want to be there. You were on your own.*

Nadler: There are only two types of people in the world: survivors and nonsurvivors. If you want to be a survivor, you have to find your way. I'm sure you did it, and I'm sure others did it in different ways. Sometimes there is more support behind you. I've had to do it on my own. I was promoted quite young, before my 45th birthday, to be a full professor. That happens rarely. I was still moonlighting in the emergency room the day I was promoted to full professor. Every Thanksgiving we had lunch/dinner early because I left for moonlighting in the emergency room. And every Christmas I moonlit to cover because I was Jewish. Every New Year's Day I was in the emergency room because they paid time and a half. I started moonlighting at Prince George's General Hospital when I was 28, and I finished moonlighting here at local New England hospitals when I was 45. I had moonlighted 3 years and 4 months nonstop, uninterrupted in the emergency room. I was a bloody good emergency room doctor. Nevertheless, that was far less painful than typing in R. R. Bowker Publishing Company.

Roberts: *What is your life like now?*

Nadler: It's very different. Now, I'm not just a lab rat. Through my entire professional life I've seen patients. That is very important to me. I see all the patients in trials that I conduct. I have been given a lot of leadership roles over time. I had the privilege of building the division of hematologic malignancies to one of the premier departments in the world. The fellows who came out of it were terrific. I was made the first major chairman of the department of adult oncology at Dana-Farber when the Brigham and Women's Hospital and Dana-Farber merged their oncology services.

To be honest, I didn't like what I had inherited. The first day I told the faculty that this place wasn't good enough to send

my family to. I indicated that the department would change, and those not willing to change would be gone. I recruited Eric Winer from Duke to lead breast cancer and Bruce Johnson from NIH to lead lung cancer. When I started, we had 27,000 outpatient visits. When I stepped down 5 years ago, we had 200,000 patients. We were losing money initially. By the time I finished we were profitable. I spent most of my time recruiting both clinicians and scientists. There are two types of people in the world: architects and builders. I'm not a good builder, but I'm a good architect. I was able to build a division and department. There is a man that I revered in my life: Eugene Braunwald, who is one of the great men of medicine and a personal friend.

Roberts: *He also is my hero.*

Nadler: Where did Eugene Braunwald's power come from? It wasn't just from his intelligence but his word. Braunwald had three answers to any question: yes, no, and "I like it but not now." And if he said "yes," his word was as good as gold.

Another man who had a great impact on me was Ramzi Cotran, a pathologist. He died a few years ago of metastatic ocular melanoma. Ramzi mentored me during my time as chairman, and he taught me that there are three stages to life. We all start at the same place. First, we are all about ourselves (the stage is call "me"). Then, you take a wife, have some children, set up a lab, and set up a small group, which becomes "us." But Ramzi was the master of "them." "Them" is the way we feel about our grandchildren. Some people, rare people, transition, so that the focus is not on themselves or their personal groups but on the next generation. Braunwald was such a person. I got that into my mind, and so about 5 years ago, in my mid-50s, I decided I did not need to try to be the best investigator in the world. It's no longer about me. I don't care. I do have a lab still because I need credibility and to stay current in science. I do see patients because I love seeing patients.

What I am really trying to do is to fix the missing link, and for me the missing link is a generation of people who don't exist right now. All across this nation, we have brilliant basic scientists and we have brilliant clinicians, but we don't have a cohort of people who can do the experiments that can take an idea from a laboratory and get it into a clinical unit. Such people are rare.

You always hear about translational research. The definition is wrong. I've worked on a definition of it and convinced everyone at Harvard, and I hope to convince everyone in America. A translational investigator is a basic scientist who has a hypothesis that can only be answered by a human experiment. The missing link is the clinical investigator. That is the person who does the experiment and takes it to the ward. At Harvard Medical School, I find <50 total translational researchers in all fields. I have been busy working at my own place creating these people from scratch. We advertise for a chemist, and we get 50 qualified people for two slots. We advertise for a clinical investigator, and we get none. These people just do not exist. We wrote an ad and stated that we had a \$2 million package to recruit translational clinical investigators for medical oncology with 5 years of protected-time salary support. We advertised all over the world for three such positions and got just two responses. My

dream for the last 10 years of my professional life is to build on Cotran's idea: "It's not about me, it's about them." Braunwald has trained a legion of these people.

I've had the privilege of meeting and knowing some of the finest people in America. Gene Braunwald said the same thing to me. Gene wrote me a short letter when I got promoted in 1992. (He was the one who promoted me.) It said, "Dear Lee, I want to explain something to you. The most important title is 'professor.' Any other title that you get is meaningless." When I got promoted to full professor, I met Dan Toteson, the dean of Harvard Medical School. I had never met him and thought he did not even know my name, but he came up to me and told me that "I was a dinosaur." I said I didn't understand. He told me I would understand some day. Now I do.

Roberts: *What have your three children done?*

Nadler: I'm very proud of them. Ellen and I have parted amicably, largely because unfortunately I can't be anybody but who I am, and she wanted somebody who was much more normal. My son, Eric, a delight, was born on January 30, 1973. He does not have his father's emptiness in his soul. He is very comfortable with who he is. People have told me he is a doctor's doctor. Eric was very good in public high school in tennis. He was not drafted by any of the Ivy League schools. He got into Wesleyan off the waiting list. The first day of college, Eric walked up to me and asked for a favor. He asked me to just say "yes" without asking what it was, so I said "yes." He said he knew that I had never bothered him about school and his grades, but for the next 4 years, he didn't want me to ask him what he was majoring in or what his grades were or how he was doing. I asked if he was kidding. He said, "Trust me."

Three years later, I didn't know what Eric was doing. Eric came to me and said he needed a summer job. He wanted me to make contact with Zeke Emanuel, who was then head of ethics at Dana-Farber, and his wife, Linda Emanuel, who ran the ethics program at the American Medical Association. He wanted to work with Linda. I said, "Okay." He talked to Zeke on the phone, and Zeke asked him for his transcript. (He didn't know about the situation that I had with my son.) I passed Zeke in the hall, and he said, "Great kid." I asked, "How so?" He looked at me. I said, "I had no clue." Eric's lowest grade ever was an A. He had lots of A+'s. His MCATs were brilliant. He wrote a thesis on genetic screening and women's rights that got the highest honors at the school. He is a brilliant writer. One part of the MCATs includes writing; he received the highest grade. I was impressed. I never said another word. My son and I are good friends.

I told Eric not to go into oncology. I tried to sell neurosurgery. He didn't pay any attention to me. I am told that they love him here at BUMC. Texas Oncology is the finest group of oncologists in America. There is no group that is close to Texas Oncology in their standards and accomplishments. They recruit the premier people out of the premium programs. Two of our premier Dana-Farber trainees had come here earlier: Estil Vance and Dave McCollum. These are Dana-Farber's best people. Marvin Stone showed me around, and I am astounded

by the research institute. I know Jacques Banchereau very well. We have been friends for over 25 years.

Roberts: *Did you see the plans for the new cancer center?*

Nadler: No. But I have known Joe Fay for 20 years.

My middle child, Sari Alison, who was born on July 14, 1976, was going to go to law school, but after working as a paralegal in New York City she hated lawyers. She returned to Boston and worked at AmeriCorps. She worked in a poor neighborhood with kids trying to improve their education. Then she got a job in development, raising money at Harvard Law School for a year or so while her future husband was still in Boston. He squeaked his way into dental school at Columbia 4 years ago. Michael is graduating in June at the top of his class. They are going to be in New York 6 more years. He placed as an oral surgeon at Columbia and will get a medical degree in addition to his DDS. He wants to be a surgeon. They got married last summer, and Sari will complete her master's degree in educational policy from Columbia and will begin teaching college in June. I am very proud of Sari and Mike.

My baby, Ruth Merrill, born February 12, 1979, is an artist and fashion designer. She went to Los Angeles for 4 years and became one of the lead designers for the Roxy Quiksilver Company. She got married two summers ago and became a mother on November 25, 2006. In August she decided to move back to Boston. She lives about 2 miles from Grandpa, and I get to hold my granddaughter often. Her husband, my son-in-law, is back in Boston, still doing finance, as he did in California.

We have a very close family. My kids are coming home this weekend. Eric's fiancée, Ann Hong Tran, is at Southwestern and is a fourth-year urology resident. She was born in Vietnam, went to Harvard College, and grew up in Houston. Her parents are first-generation Vietnamese and work in factories. They are extraordinary people, embody family, and supported Hong through Harvard College. Southwestern says she is the best urology resident they have ever seen. I've been blessed. I have great kids, and I now have three more great kids.

Roberts: *Do you like being a grandfather?*

Nadler: It is a privilege to live to see your grandchildren.

Roberts: *What time do you get up every morning?*

Nadler: 4:30 AM.

Roberts: *You get to work at what time?*

Nadler: I go to the gym at 5:30 every morning and get to work at 7:00 AM.

Roberts: *What time do you go home?*

Nadler: The earliest is 6:00 PM and the latest, 10:00 PM.

Roberts: *Do you have any hobbies outside of medicine?*

Nadler: I exercise. I spend time with my close friends. I collect art. I collect microscopes, as does Marvin Stone. Between Adrian Flatt's hands and Marvin Stone's microscopes, I'm blown away by the sensitivity of art at BUMC. I'm becoming more interested in art now—not the old-fashioned stuff but glass art. I didn't spend enough time collecting friends, so I'm collecting those now.

Roberts: *You have been a great interviewee.*

Nadler: Thank you.