As Brad Berk sees it, “All the work I do can pretty much fit under the heading of signal transduction in blood vessels.” This deceptively short phrase, however, covers decades of research into the cellular and genetic mechanisms that produce some of cardiovascular medicine’s most stubborn challenges: atherosclerosis, aneurysms, and pulmonary hypertension. Berk’s academic career has led him from the University of Rochester to Harvard Medical School, Emory University, and the University of Washington before circling back to Rochester. Currently, he holds the post of Distinguished University Professor in medicine, neurology, pathology, and pharmacology and physiology. He has founded and directed 2 multidepartment institutes: the Aab Cardiovascular Research Institute (CVRI; from 1999 to 2006) and the University of Rochester Neurorestoration Institute (URNI; from 2015 to the present).

While at the University of Washington, in 1998, he published with Oren Traub a review of what was then known about how changes in blood-flow profile (steady versus disturbed) influence vascular disease. Berk went on to develop a highly reproducible model for vascular remodeling of the carotid as mediated by blood-flow profile. The disturbed flow region shows the formation of intima—a pathological thickening of the vessel wall. Because this thickening is predictive for cardiovascular events, the identification of genetic factors that played a role in the process marked a significant advance in cardiovascular research.

Together with Korshunov et al, Berk studied 3 disease processes that contribute to intima: endothelial dysfunction, inflammation, and smooth muscle growth. By performing a genetic linkage study to home in on regions of the mouse genome that contribute to the intima, Berk and Korshunov identified a specific gene (RpL17) that accounts for smooth muscle cell growth. With Smolock et al, they found a key link to inflammation now identified with a gene (Pnpt1) and showed that this gene regulates endothelial activation and permeability.

Berk has also extensively studied the role of oxidative stress in cardiovascular disease. Together with two excellent scientists in his laboratory, Duan-Fang Liao and Zheng-gen Jin, he identified cyclophilin A as a factor secreted from cells in response to oxidative stress. This research team also showed that cyclophilin A, when added to smooth muscle cells, prevented apoptosis and stimulated proliferation, but when added to endothelial cells, it promoted apoptosis. Cyclophilin A has been found to play a pathogenic role in intima formation, aneurysms, atherosclerosis, cardiac hypertrophy, and increased blood–brain barrier permeability.

Does a Scientific Turn of Mind Run in Your Family?
I think you could say that. My dad was a chemical engineer, and my sister became an electric engineer. My dad was a big fan of science fiction magazines, and I grew up reading them. It was the start of the Space Program, so I would clip out front-page articles of every launch (especially the Gemini and Apollo missions) and save them in a notebook. Scientific news—new elements, cosmic microwaves, and the Big Bang theory, fossil discoveries of new animals—was everywhere.

What Made You Want to Become a Scientist?
I became interested in science at a very early age, partly because of the Space Program, but also because of my childhood experiences with nature. I lived in a fairly undeveloped part of Rochester, so my friends and I would go into the woods to eat wild berries, find birds’ eggs, and catch all kinds of animals—especially snakes to scare my sisters and tadpoles to keep until they became frogs. I read about these animals in the encyclopedia and developed an affinity for biology.

In high school, I took some of the first Advanced Placement courses that were being offered, in math and in chemistry. The course in chemistry was particularly stimulating, since we had our own laboratory that we could go to any time, and—best of all—without supervision. While cooking cans of soup on Bunsen burners was fun, synthesizing dyes and combustible compounds was much better. The six other Advanced Placement Chemistry students and I wrote a grant (application) to the local science museum to build a spectrometer, so that we could analyze our compounds. The good news is that we had parents who were...
engineers and a dentist, who could help us with the wiring and build the device. When it came time to go to college, I looked at schools that were strong in science, but most of them seemed too one-sided. Instead, I went to Amherst College—a liberal arts school in Massachusetts—where I studied history along with biology. For my senior thesis, I wrote about Trofim Denisovich Lysenko—a very influential scientist in the Soviet Union—who held that Mendel was wrong and that Lamarck—with his theory about the inheritance of acquired characteristics—was correct.

**At What Point Did You Start Focusing on Medical Research and on Cardiology, in Particular?**

When I was applying to medical schools, I was still trying to decide whether to do research or clinical work. I was excited to find that there was an ideal solution: the Medical Science Training Program, which combined research and clinical education. I chose the one at the University of Rochester because it had a strong biochemistry department, but I did my graduate work in the pharmacology department because my thesis advisor, Patty Hinkle, was a very talented, passionate, and down-to-earth scientist. She had just finished a postdoc at Harvard, where she had worked on thyrotropin-releasing hormone receptors and signal transduction. This area seemed likely to yield many important discoveries in human disease.

When I finished my MD–PhD, I was excited to match for my internal medical training at the Brigham and Women’s Hospital in Boston because there were many other MD–PhDs there. After my residency, I stayed at the Brigham for subspecialty training in cardiology. I was fortunate to begin work as a postdoctoral fellow at Harvard with two well-known physician scientists, R. Wayne Alexander and Mike Gimbrone. They were pioneers in vascular biology and also studied signal transduction, which matched well with my PhD work. Our first publication was in Science in 1986, and together, we published five papers in two years.

Clinically, I was attracted to cardiology because I loved listening to heart murmurs. People choose a career in medicine because they want to help other people, and they pick a particular field because they are good at it. I have a good ear for sounds: when I put my stethoscope to a patient’s chest I heard what sounded like a symphony, whereas other students heard the sound of rushing water—if they were lucky.

As a resident, I was fortunate to work with some truly eminent cardiologists, including Wayne Alexander, Tom Smith, and Eugene Braunwald. Braunwald was the editor of “Harrison’s Principles of Internal Medicine” and the author of “Braunwald’s Heart Disease”; both are among the preeminent books in their field. I think I got hooked on cardiology working with these cardiologists, each of whom was an excellent mentor in academic medicine. It was also an exciting time in the field, with the advent of balloon angioplasty, stents, implantable defibrillators, and new drugs for hypertension, hyperlipidemia, and congestive heart failure.

And cardiology is one of those fields that are still making enormous advances today.

**One of Your Roles at Rochester Has Been as CEO of the Entire Research and Clinical Enterprise. How Did That Come About?**

I had a very substantial administrative career, which is different from many researchers. The administrative side of my work has taken place mainly at Rochester: I chaired the cardiology unit from 1998 to 2003, and then, starting in 1999, the department of medicine. In 2006, I was chosen after a national search to be CEO of the Medical Center. We have a very centralized system here because all medical programs report to the CEO, including the five hospitals, the research and clinical facilities, and the schools of Medicine, Nursing, and Dentistry. This role requires an enormous time commitment, so I decreased my research effort to 15% of my time.

**Launching the Neurorestoration Institute Seems to Have Been a Departure From Your Usual Line of Work—What Is the Story Behind That?**

In 2009, I suffered a severe spinal cord injury (C4–C5 incomplete, making me a tetraplegic) as the result of a bicycle accident. I was in the hospital for 119 days and out of work for almost a year. As a result of the fantastic care I received during my surgery, hospitalization, and rehabilitation, I was able to return as the CEO. I had three major projects to finish: implementation of an electronic medical record, introduction of a Patient- and Family-Centered Care Program, and construction of the new Golisano Children’s Hospital.

Once these projects were finished, in 2015, I stepped down as CEO to develop the URNI. This institute will have two major functions. One is to house translational and clinical trials for individuals with acute neurological injuries (spinal cord injury, stroke, and traumatic brain injury), and the other is to be the physical site for multidisciplinary care for these individuals. This project is obviously very meaningful to me personally, but from my own experiences, I believe that we can provide much better and more comprehensive care. The concept underlying the URNI is that by bringing specialized health providers, resources for rehabilitation, and investigators involved in clinical trials all together in one physical location, we can offer patients a better diagnosis and treatment plan. Specifically, individuals with these neurological injuries will see appropriate specialists—neurologists, physiatrists, occupational and physical therapists, pain specialists, bowel and bladder specialists, and integrative medicine providers during a one- to two-day visit. At the end of the visit, a comprehensive plan, including eligibility for clinical trials, will be provided and discussed with the patient and family.

**How Do You Divide up Your Time on a Typical Workday?**

I have a regular routine that I follow each day. I get to the office each morning around 9:00 AM. After a brief review of the calendar and important projects for the day, I use a stationary bicycle next to my desk and pedal for 50 minutes while answering e-mails. Then I work on a self-help book that I am writing or on grant applications. I perform rehab exercises for an hour, then eat lunch, and usually go to a noon seminar or meet with faculty who will participate in the URNI. Later in the day, I visit the laboratory to review the day’s experiments and discuss results and plans for the next day. As a summary, I spend 35% to 45% of my time on research, another 35% working on my book, and the rest of my time developing programs for the URNI.

And speaking of neurorestoration and rehabilitation, I want to mention something that a lot of people do not know: the National Institutes of Health has supplementary grants to help cover the extra expenses of people with disabilities.

In 1990, the first President Bush signed the Americans with Disabilities Act (ADA), which has transformed America. And you know, disability comes in all different forms: a person could be blind or deaf or have cerebral palsy or multiple sclerosis or any of a thousand other things. At the National Institutes of Health, they...
have a whole grants program to accommodate researchers with disabilities, for which you have to write a separate application with a budget, specifying the accommodations you would need and the estimated cost. The ADA costs quite a lot of money—any company with more than fifteen employees has to comply—but it means a huge pool of talent and labor is not lost to the country because of disability.

How Big a Role Has Plain Old Hard Work Played in Your Success?
Plain old hard work is a lot of it. You have to read the literature, you have to go to the meetings and the seminars. But also you have to talk to people and exchange ideas. To me, one of the key aspects of science is the opportunity to bounce ideas off your colleagues. At the Aab CVRI, we have a Friday lunch meeting during which faculty members can present their work in progress or their grant renewals and revisions. The feedback they receive is valuable for them, but the process is valuable for everyone because we learn about each other’s science and we learn how to write successful grant applications. In my laboratory, we meet every Tuesday to talk about our recent experiments in a very critical manner, going through the original data and working on people’s presentation skills, which is especially important for the graduate students. These meetings are essential for designing better experiments and coming up with new ideas.

Do You Have Any Advice for Young People Who Are Considering a Career in Scientific Research or Just Starting Such a Career?
I would tell them to pick a good question, a big question. Do not pigeonhole yourself. Do not do incremental science; it is not satisfying, and it does not get you funding. But it has to be something that you are genuinely curious about. For me, as an example, instead of saying, “I want to work on pulmonary hypertension”—which is certainly a big topic and an important one—I said, “I want to find out about signal transduction in blood vessels, but especially what differences in endothelial cell biology make tissue-specific diseases.” What I ask my postdocs is, “If you were going to give a plenary lecture five years from now, what would you want to be talking about?”

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None.

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