Profiles in Cardiovascular Science

Victor Dzau
Cardiovascular Physician Scientist Takes Helm at IOM

Susan Ince

A fter a 4-decade career combining medicine, basic and translational science, administration, drug development, and health policy, cardiologist Victor Dzau, MD, has begun a 6-year term as the eighth president of the Institute of Medicine (IOM) and will become the first president of the National Academy of Medicine when the IOM changes status in July.

Dzau, chancellor emeritus of Duke University and previously president and CEO of the Duke University Health System, took a leave of absence from Duke to serve the IOM in its mission to address the larger problems of medicine and health care, but he has no intention of giving up his laboratory.

“Many people think I’m insane to continue to do science and deal with the time demands, the competition and the headaches of grant funding. But I will continue because I love it. It’s what I live for. And I want to be a good role model, to understand the challenges scientists have, so I can be a better person to serve the nation in my capacity at the IOM,” says Dzau.

Multitasking has been a constant in Dzau’s busy career. While serving as chief medical resident at Peter Bent Brigham Hospital in Boston under Eugene Braunwald, Dzau simultaneously conducted research as a postdoctoral fellow in physiology at Harvard University and cardiac biochemistry at Massachusetts General Hospital. There he purified and cloned renin and later used an experimental angiotensin-converting enzyme (ACE) inhibitor in treating human heart failure. He pioneered the concept of the tissue angiotensin system—the now widely accepted idea that angiotensin’s influence was not simply because of the circulating hormone, but instead to angiotensin produced and functioning within cardiac, vascular, and renal tissues. He also pioneered gene therapy for vascular disease, and his recent work on stem cell paracrine mechanisms and the use of microRNA in direct reprogramming provides novel insight into stem cell biology and regenerative medicine.

While devoting much of his career to translational research, Dzau was recognized early on for his leadership abilities and eventually chaired the departments of medicine at Stanford University School of Medicine and Harvard’s Brigham and Women’s Hospital in Boston. He has founded 3 companies and served on the boards of numerous others. In addition to his work at the IOM, he chaired the National Institutes of Health Cardiovascular Advisory Committee and the Association of Academic Health Centers.

Working both locally and globally, Dzau endeavors to improve healthcare access and health literacy. In Durham County, an area with great economic and health disparities, he helped form Project Access to bring specialty care to people without health insurance. He created the Division of Global Health Equity at Brigham and Women’s Hospital and the Duke Global Health Institute. He chaired the Global Agenda Council on Personalized and Precision Medicine for the World Economic Forum, and cofounded and chairs the International Partnership for Innovative Healthcare Delivery.

Dzau is a senior consulting editor of Circulation Research. In a recent interview with the journal, Dzau discussed his journey from Shanghai to Washington, DC.

Tell Me About Your Childhood
I was born in Shanghai. During the communist takeover, it was a very difficult time for my family because my father was a target of criticism for owning a factory. We fled in 1950, telling people we were going away for the weekend but going south and crossing into Hong Kong, pretty much giving up everything. Initially it was very tough for us, with the whole family living in a single room while we tried to reroot ourselves and

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find financial stability. The effect on me was that the poverty and health inequities I observed in postwar China, including Hong Kong, drove me to become a physician.

How Did You End Up at McGill?
I chose to go overseas because, in the 1960s, Hong Kong was not a major educational hub. I ended up in Canada because I wanted to be a physician, and if you were educated in a commonwealth country, you could come back to Hong Kong to practice, but if you went to the United States, you probably could not.

Like all good Chinese families to whom education is everything, they put all their money together and, at the age of 18 years, I was fortunate enough to go to McGill for an undergraduate biology major and then medical school. It was a great decision.

How Did You Start Doing Laboratory Science?
The start of my science journey was after my first year at McGill, when all my friends left for the summer and I needed to find a job. I found a listing from Royal Victoria Hospital looking for someone to work on the physiology of hyperglycemic coma. John Dossiter, a urologist, and Hanna Pappius, a neurochemist, gave me a chance to work in the laboratory even though I had no experience whatsoever in science. I was brought up traditionally Chinese, so to be welcomed with the Western approaches of openness and inclusiveness was an eye-opening experience for me. Pappius became a mentor, and that mentorship lasted through undergraduate years and helped me go to medical school. Also, McGill was very Oslerian, and William Osler very much believed in the scientific basis of disease, so that informed me as well.

How Did You Get Interested in Cardiovascular Medicine and Research?
In the physiology course in medical school, when they taught cardiovascular physiology, particularly discussing the hemodynamics of aortic stenosis, I was truly energized. It seemed like this was an area where medicine and science came together.

When I was a medical resident at Peter Bent Brigham Hospital in Boston, I told my mentor Eugene Braunwald that I would like to work in hypertension. He said that there were only 3 places to consider going after my residency, and one was to stay at Harvard to work with Ed Haber and Cliff Barger. They were working together on the idea of blocking renin angiotensin to show how important it is physiologically and to also think about future therapy.

My project was to purify renin. These were the days of gel filtration and ion exchange columns, and it took me 3 years and grinding up many, many kidneys to come up with a tiny bit of this enzyme and make an antibody to it. When we published that first article in Science, it opened the door for me as a cardiovascular researcher.

Upon purification, we recognized that renin was a very unstable enzyme that would require very specific blockers, suggesting that renin inhibitors would not be as easy to use as ACE inhibitors and angiotensin receptor blockers. Ed Haber went on to synthesize his own antagonist to ACE, which was a nanopeptide that had to be given intravenously, and later on Squibb developed captopril as an oral agent.

What Was Your First Experience With Clinical Research?
This was at a time when we had nothing to give people with heart failure except digitalis, diuretics, or applying tourniquets to reduce venous return. While I was a chief resident at Peter Bent Brigham Hospital, I worked with Norm Hollenberg and Gordon Williams and gave an experimental intravenous ACE inhibitor to patients who were very sick, mentally clouded with end-stage heart failure, and approaching death. The response was dramatic. I remember one patient who was so sick that he could not lie down and instead slept sitting up with his head resting on the table. A week after we gave him the ACE inhibitor, he improved dramatically and was able to leave the hospital. He had no money on admission, and as he was being discharged, I offered to give him money for a taxi. But he reached into his pocket and pulled out a new bundle of cash—his mind had cleared so much he had been winning at card games with other patients! My entire career was influenced by these early experiences of bringing basic and molecular research to patient care.

Tell Me About Your Attempts to Apply Gene Therapy to Cardiovascular Disease
When I went to Stanford in 1990, I was really taken by the idea of gene therapy and wrote a series of articles predicting how it might change the management of coronary artery disease. My team was among the first to develop DNA decoy therapy to inhibit neointimal hyperplasia and accelerated atherosclerosis that can lead to the failure of vascular bypass grafts.

We founded Corgentech and took this all the way to phase III trials to prevent graft failure, but the results were not positive, despite the encouraging results in phase I and phase II. With hindsight, although our concept was correct, the single dose of DNA decoy did not have a long enough duration of effect to prevent graft stenosis 6 months later.

Meanwhile our group, with Randall Morris, was showing that rapamycin inhibited smooth muscle proliferation. Andrew Marks, of Columbia University, took that work a lot farther, eventually leading to the developing of drug-eluting stents. At that point, everybody abandoned the idea of gene therapy and went to drug-eluting stents to prevent restenosis. So the concepts we had stalled, but we continued the work on gene therapy and developed the idea of protecting the ischemic myocardium, which is still relevant today and we are still trying to apply this approach to humans.

Could You Describe Your Recent Work on Stem Cell Action and Therapy?
That has been the basis of my work for the past 10 years or so. In attempts to use genetically engineered mesenchymal stem cells to treat myocardial infarction, the question emerged: Why do stem cells work when they all die very quickly after you inject them? We pioneered the paracrine hypothesis, that stem cells exert their repair and regenerative actions by secreting signaling molecules that change the behavior of nearby cells. That raises the potential of using these paracrine factors themselves as therapeutic agents. We have injected the medium surrounding stem cells into animals with the aim of identifying the molecules made by stem cells that could be used for treatment to
What Would You Tell a Young Person It Takes to Be Successful in Science?

I would say opportunities open if you follow your passion and put your effort into what you are good at and care about. I would tell a young person that one cannot really engineer one’s career. For me, things just happened because I followed my passion; I always put every ounce of effort into doing the best work, and I had people who recognized my potential and gave me a chance.

I am actually encouraged by the younger generation of multitaskers now in college. Our generation was told you can only get things done if you focus. Although that is a good advice, I also believe multitaskers may be able to see more possibilities and take more risks. The key for multitaskers is to complete all your tasks with excellence and avoid becoming diffuse or distracted.

As you pursue the things you love, success comes easier and things come along that expand your universe and doors open to you—I certainly never thought that I would be working in policy. I tell young people that what you learn in science can influence not just your laboratory work but the way you look at life and the way you can help the nation with science policy and advice.

What Are Some of Your Goals for Your Time at the IOM and the National Academy of Medicine?

The IOM is an independent, nonprofit organization that works outside of government to provide unbiased and authoritative advice to decision makers and the public on important matters science and medicine. The New York Times describes the IOM as the most esteemed and authoritative adviser on issues of health and medicine, and its reports can transform medical thinking around the world. What the institute also does well is convening, through its forums and roundtables, the best minds and world’s experts to discuss and debate important and complex issues.

As we approach 45 years since our founding, IOM must think strategically and creatively to continue making a positive difference to the world we live in. I hope that we can make the IOM more innovative and action oriented. I would like to develop more strategic relationships with organizations that have the ability to implement the strategies and services proposed by the IOM.

My vision for the IOM is centered around three goals: advance science and its application; respond to top priorities in health and healthcare; and lead and inspire for the future. What I hope to achieve is for IOM to be the voice for the nation’s aspirational goals in science, medicine, and health. For too long we have hunkered down and stopped aspiring. IOM should bring everyone together to identify grand challenges and ambitious goals and to define collective solutions. Like a mini-moonshot, I hope we can bring together science and government and industry to collectively address important issues in health and medicine.

Disclosures

None.
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