

## A tale of two callings

Robert J. Lefkowitz

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### Supplement

First, I want to thank Ralph for that wonderful presentation. After listening to all that, I can hardly wait to hear what I am going to say. Preparing these Kober Medal presentations requires a tremendous amount of work. When I first asked Ralph if he would do me the honor of making these remarks, he asked if I had any guidelines I wanted to give him. I responded: Ralph you know that I would want something simple and modest — not overly ostentatious or hagiographic — no matter how long it takes. Seriously though, Ralph has been my closest friend for more than 30 years, and I am in his debt for this. All the more meaningful to share this wonderful moment with a number of family members, including, amongst others, three of my five children, two of my four grandchildren, some in-laws, and my wife, Lynn. As they say, behind every successful man stands a surprised woman. Her constant and loving support is one of my true blessings. The Kober Medal has such a special place in our profession that, despite more than a year to accomplish the task, I continue to have difficulty getting my head around the notion that I am joining the ranks of its recipients. For the more than 40 years that I have attended [...]

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## Acceptance of the 2011 George M. Kober Medal

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The Kober Medal has such a special place in our profession that, despite more than a year to accomplish the task, I continue to have difficulty getting my head around the notion that I am joining the ranks of its recipients. For the more than 40 years that I have attended these meetings, the Kober Medal presentation to a series of individuals I viewed as iconic heroes has always been a highlight for me, something I would never miss, a yearly source of inspiration and delight. So, despite my very real qualms about assuming a place in this pantheon, I will for the moment adopt the philosophy of “fake it until you make it.”

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**Figure 1**

Two future Kober Medalists: Joe “Butch” Goldstein (left) and Bob “Sundance” Lefkowitz (right). Note that Lefkowitz is outgunned by Goldstein, but then, who isn’t?

As a young child growing up in New York City, I was very prone to hero worship. I mention this because I have been struck in recent years by a remarkable commonality apparent in the earliest aspirations of several Kober medalists as presented at this meeting. This picture depicts a young Joe Goldstein, a recent Kober medalist and former Nobel laureate, that was shown by Jean Wilson when he presented the Kober Medal to Mike Brown and Joe a few years back (Figure 1). Unlike myself, Joe grew up in a small town in South Carolina. Now, compare this photo of me taken at about the same time on the streets of the Bronx. This series of  $N = 2$  has suggested to me that an early admiration for Western heroes may be a stepping stone to the Kober Medal later in life, regardless of the widely divergent cultural context in which the winners may have grown up.

At about the same time that these photos were taken, one of my most important heroes was my family physician, a man named Dr. Joseph Feibush. He was a general practitioner who made house calls and made me feel better when I was sick. By the third grade I was quite convinced I wanted

to grow up to be just like him, a practicing physician who healed the sick. From then on I also loved reading books about doctors, especially novels in which an MD played a central, usually heroic, role.

This brings me to another point – how remarkably fortunate I have been to experience my life’s work as a calling. Not only did this sense of a calling to clinical medicine clarify and direct my early years through medical school and residency, but it certainly saved me all the anguish that many young people seem to face in finding their way in adult society.

But I have been doubly fortunate in this regard in that I would subsequently feel a second calling, one to scientific research. I would never have imagined this during medical school and house staff days. I was totally devoted to clinical work and avoided all research electives in medical school to focus on clinical activities. Nonetheless, two of my professors at Columbia College of Physicians and Surgeons who had the most pronounced influence on me were Paul Marks and Dickinson Richards, himself a former Kober and Nobel medalist for his role in developing cardiac



**Figure 2**

“Nothing is impossible for the man who doesn’t have to do it for himself.” Some trainees of the author at his 60th birthday celebration.

catheterization. These two men introduced me to a way of bringing scholarly scientific findings to the bedside of sick patients, which really began to awaken a dormant scientific curiosity in me.

As with so many physicians of my generation, my two-year experience as an officer in the United States Public Health Service at the NIH from 1968 to 1970 in fulfillment of my draft obligation forever altered the path of my career. In the laboratory, I made a remarkably slow start. Lacking in basic laboratory experience and technique as well as the necessary patience and perspective, my fledgling attempts at research met with unrelenting failure during my first 18 months there. It was during this time of failure and frustration that I made arrangements to return to full-time residency and then cardiology fellowship at the MGH to follow my two-year stint in Bethesda. I had never really failed at anything before so this was a new experience for me, but one which would help me in later years to advise my own trainees. However, I was fortunate during this period to have two wonderful mentors, both members of this association. My spirits were continuously elevated by the unflagging and buoyant enthusiasm of Jesse Roth, even while I was continu-

ously brought down to earth by the rigorous temperament of Ira Pastan, who never failed to point out the key controls missing from my experimental design, which generally invalidated my conclusions.

Somewhere around the 18-month mark, I finally began to make some progress, and things started to turn around. Though tempted to extend my time at the NIH, I honored my commitment to the MGH, and so after the two-year assignment, I headed off to residency again.

The next six months were absolutely pivotal for me. I threw myself into the clinical work with my usual fervor. But something was missing. For the first time in several years I had no data. I was like a junkie who needed a fix. As I thought back to the dark days of my failing experiments during my first year at the NIH, I had the epiphany that even negative data was better than no data.

The second six months of my senior residency year was supposed to consist of elective rotations. House rules prohibited residents from working in research labs since they were paid with clinical dollars. Nonetheless I arranged to surreptitiously do research in the lab of the late Edgar Haber, Chief of Cardiology. His

labs were located deep in the basement of the Bullfinch Building. I got away with it for a while. Then, late one cold winter night, the residency director, Dan Federman, was taking a shortcut to the parking lot through tunnels that wound past Ed’s lab. He caught me walking in the hallway carrying a rack of test tubes. Waving a finger in my face, he said, “Lefkowitz, I heard rumors that you were doing research, see me in my office tomorrow.” The next day, he and Alex Leaf, Chairman of the Department of Medicine, gently upbraided me, but it was just a slap on the wrist, and they never really ordered me to desist, which is what I had feared. I continued my research in Ed’s lab throughout my cardiology fellowship over the next two years, and it was here that I initiated my work on the adrenergic receptors.

I moved to Duke in June of 1973, recruited by the Chief of Cardiology, Andy Wallace, and the Chairman of Medicine, Jim Wyngaarden. They wanted me to start a program in Molecular Cardiology. They both kept a helpful and supportive eye on me the first few years, reading my grant applications and in Jim’s case actually reviewing my research findings a couple of times a year.



I would be remiss if I did not acknowledge the two major sources which have funded my research. First is the NIH R01 grant mechanism. My first R01 has been active for almost 40 years now. And then, of course, there is the Howard Hughes Medical Institute (HHMI). I became a Hughes investigator in 1976, so that my tenure with the organization is now 35 years and counting. I have served under every research director and president that the institute has had, beginning with George Thorn. It is truly a remarkable organization which has

enabled much of what I have been able to accomplish. Alas, however, fewer and fewer of the investigators today are physicians.

It's hard for me to believe that I have been at Duke for almost 40 years now. During that time about 200 fellows and students have worked with me in the laboratory. A dozen of these are members of this association. Mentoring these trainees has been one of the greatest joys of my professional career. And I watch their independent careers evolve with extraordinary pride in their subsequent accomplishments.

And, on this note, it seems to me appropriate that I conclude these brief remarks by highlighting this extraordinary group of individuals. This photo was taken eight years ago when about half of my trainees up to that time returned for my 60th birthday party (Figure 2). As you look at this, I think you will be able to understand what is undoubtedly at the core of whatever success I may have achieved in my career. It is simply this: "Nothing is impossible for the man who doesn't have to do it for himself." Thank you very much.