

Michael Brown and Joseph Goldstein: Tribute to my inspiration

The strength of scientists lies in touching the lives of millions through their inventions as well as encouraging young minds to follow their lead. I was a teenager when I first came across the scientific contributions of Dr. Michael Brown and Dr. Joseph Goldstein and have always considered them as an inseparable scientific pair who heavily influenced my academic career and personal life.

Growing up in India in an era of burgeoning globalization, I have witnessed the growing burden of cardiovascular disease in a developing nation. Just like the legend of Kisa Gotami who was asked by Buddha to bring a mustard seed from a household that has not witnessed death in an attempt to instill the idea of death as an inevitability, it would have been equally difficult to find a family that has not witnessed cardiovascular events in its near and dear ones. On a personal note, I had also lost my high school science teacher, a man in his early 40s, to myocardial infarction. Despite his elevated blood low density lipoprotein cholesterol (LDL-c), he was non-compliant on his statin medication. I have always nurtured a desire to become a preventive cardiologist, ever since. Statins have become the cornerstone of preventive cardiology. Not surprisingly, the discovery of statins based on the seminal scientific work of Brown and Goldstein caught my imagination at a very tender age.

Physician scientists play a role analogous to that of the Rosetta Stone: they help bridge the gap in understanding and communication between the two interconnected 'languages' of clinical medicine and biomedical research. Brown and Goldstein are epitomized as model physician scientists. Their discoveries concerning the molecular basis of familial hypercholesterolemia, a single gene disorder of cholesterol metabolism, elucidated the basic biology of cholesterol transport, and provided a prime example of translational research, years before the term was actually coined. My enthusiasm for pursuing a career as a physician scientist during my medical school training was largely based on curiosity that developed from their work on receptor-

mediated endocytosis in our biochemistry and physiology textbooks. Taking confidence from the fact that Brown and Goldstein did not undergo a formal graduate school training to achieve their scientific goals, I accepted the position of postdoctoral research fellow in the Division of Cardiology in Massachusetts General Hospital (MGH) after the completion of my medical school training despite having minimal prior laboratory experience.

Mentorship is a key component of scientific and academic development. I believe that a strong mentor-mentee relationship helps foster a scientific ecosystem that can drive the scientific wheel forward. At MGH I investigated the role of extracellular vesicles in cardiac biology.

Coincidentally, one of the pioneers in the area vesicle biology and trafficking is Dr. Thomas Sudhof, who was a post-doctoral trainee in Brown and Goldstein's lab. Contemporary studies demonstrating the success of PCSK9 inhibitors in reducing LDL-c and improving cardiovascular outcomes were being reported and the genetic basis of that discovery was formulated by a former trainee in Brown and Goldstein's lab, Dr. Helen Hobbs and Dr. Jonathan Cohen.

Convinced that the Department of Molecular Genetics at the University of Texas Southwestern Medical Center (UTSW) chaired by Brown and Goldstein would provide an enviable environment I applied to the graduate program at UT Southwestern. I was fortunate enough to be accepted, and I am currently a graduate student in the Hobbs-Cohen lab. In a sense, life has come a full circle to me. Observing Dr. Brown and Dr. Goldstein, who inspired me to follow the path that I have undertaken, from closer quarters in department seminars and across the hallway, I feel equally humbled and privileged at the same time.

Finally, I would also highlight the profound effects of the scientific partnership of Brown and Goldstein had in my personal and professional life. Coming from a predominantly collectivist culture, I have struggled to absorb the individualistic nature of modern American society. While academic clinical training fosters collaboration and brotherhood among its trainees, few such avenues exist in training of academic science. Naturally, these dilemmas transcended the

boundaries of my personal and professional life. Role models serve to allay the anxiety and mental conundrum by providing a working module. The lasting scientific partnership of Brown and Goldstein served such a purpose, which was reflected in successful scientific pairing in UTSW which even included my mentors. Being a member of that collaborative ecosystem, I have been successful in identifying the importance of selective collectivism among individualism in academic science, thereby hastening my scientific cultural integration in a foreign country and alien work environment.

Brown and Goldstein, through their scientific contribution and partnership has been instrumental in shaping my academic career and continues to inspire my quest for scientific proficiency.