

2010 Association of American Physicians George M. Kober Medal

Introduction of Stuart Kornfeld

Ajit Varki

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AAP Kober Medal

President Horwitz, Members of the AAP, Ladies and Gentlemen: it is a great pleasure and a very special honor to present the prestigious Kober Medal to Stuart Kornfeld, the very model of the quintessential physician-scientist. Growing up with the ancient traditions of India, I learned the significance of the Guru-Shishya relationship (1), in which the Guru (teacher) is the one who has great knowledge, wisdom, and authority in a certain area and uses it to guide others — and the Shishya is the student or disciple. The principle is that subtle or advanced knowledge is best conveyed through a strong human relationship based on the student's respect and on the personal instruction by which the student eventually masters the knowledge that the Guru embodies. It is indeed a privilege to be able to publicly honor my own Guru, mentor, and scientific hero. Stuart Arthur Kornfeld was born on October 4, 1936, in St. Louis, to Ruth Baum Kornfeld and Max Kornfeld. His father was a dentist who achieved prominence in practice, teaching, and writing, authoring a much-used textbook for dental surgery. Stuart grew up attending public schools and excelling at both sports and academics. With his parents' encouragement, he decided to become a physician and a scientist. He first went to Dartmouth College in New Hampshire, graduating in 1958, and [...]

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It is indeed a privilege to be able to publicly honor my own Guru, mentor, and scientific hero. Stuart Arthur Kornfeld was born on October 4, 1936, in St. Louis, to Ruth Baum Kornfeld and Max Kornfeld. His father was a dentist who achieved prominence in practice, teaching, and writing, authoring a much-used textbook for dental surgery. Stuart grew up attending public schools and excelling at both sports and academics. With his parents' encouragement, he decided to become a physician and a scientist. He first went to Dartmouth College in New Hampshire, graduating in 1958, and then to Washington University School of Medicine back in St. Louis, graduating in 1962 (Figure 1). It was at "Wash U" that he met Rosalind Hauk in the summer of 1958, while working in Luis Glaser's lab, where she was enrolled as a PhD student. They were married a year later, in June 1959 (Figure 2). Their first child, Kathy, was born in 1960, followed by son Kerry in 1962. Their daughter Carolyn was then born in

1965, while the couple was at the NIH for two years, doing postdoctoral fellowships with Victor Ginsburg. They returned to St. Louis in June 1965 and went back to work at Washington University.



Figure 1
Graduation from Washington University School of Medicine, 1962.

Under the guidance of the legendary Carl Moore, Stuart rose very rapidly through the ranks, achieving full Professorship of Medicine in a scant 6 years, a position he still holds today. Not many people go from college graduate to full professor in 14 years! As with his academic achievements, Stuart Kornfeld's honors came naturally, easily, and rapidly, with election to the American Society for Clinical Investigation in 1972 and the Association of American Physicians in 1976. He was inducted into the National Academy of Sciences in 1982 well before the age of 50 (fittingly, in the year the St. Louis Cardinals won the World Series, an event which I think brought equal joy to Stuart). Soon afterward, he was elected to the Institute of Medicine in 1983 and to the American Academy of Arts and Sciences in 1984. This was followed by many more honors, which are listed in Table 1.

No description of Stuart Kornfeld's career can be complete without emphasizing the two individuals who most greatly influenced it. First and foremost of course was his late wife, Rosalind Hauk Kornfeld. They first met when doing science and continued to do science together for the great bulk of their careers until Rosalind's unfortunate early demise. Having been

through the Kornfeld lab, I can attest that they complemented each other perfectly and that the training that fortunate individuals like myself received was as much from Rosalind as from Stuart. And of course, there are several papers on which they are co-authors, including a 1985 classic review (2) that has been cited more than 3,600 times and is still being cited. I do remember an unusual exception, when their son Kerry came into the lab for a summer high school project and basically completed a paper for the *JBC*, working also with Marc Reitman, a talented MD/PhD student. The resulting manuscript initially listed three Kornfelds. Stuart then withdrew his name from the author list (3), saying that there were too many Kornfelds on the paper! Rosalind's career has been memorialized in many ways, including a special award in her name given by the Society for Glycobiology, for lifetime achievement in the field.

The second great influence on Stuart was his friend, colleague, and long-time Co-director of Hematology and Oncology at Wash U, Philip W. Majerus (Figure 3). One simply has to say the phrase "Stuart and Phil" anywhere in American biomedical circles, and everyone knows exactly whom you are talking about. Truth be told, it is hard to think of a greater contrast between two individuals in terms of



Figure 2
Wedding day in Bethesda, June, 1959.

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Table 1
Major honors and awards

1970	Elected Member, American Society for Clinical Investigation
1976	Elected Member, Association of American Physicians
1982	Elected Member, National Academy of Sciences
1983	Elected Member, Institute of Medicine
1984	Elected Fellow, American Academy of Arts and Science
1987	Foreign Member, Finnish Society of Sciences and Letters
1987	Alumni/Faculty Award, Washington University
1989	Jubilee Lecturer and Harden Medallist, The Biochemical Society
1991	Passano Award (with William Sly)
1992	E. Donnall Thomas Prize, American Society of Hematology
1999	Karl Meyer Award, Society for Glycobiology
2000	David C. and Betty Farrell Distinguished Professor of Medicine
2002	UCSD/Nature Medicine Mentorship Award
2002	Gerty & Carl Cori Faculty Award, Washington University
2003	Second Century Award, Washington University

their demeanor and style. But remarkably, or perhaps because of their very divergent personalities, they got on together famously and seemed to agree on almost everything. They both turned down many offers for higher-level positions in academia and stayed together as co-heads of the Division until very recently, a truly unusual and remarkable academic collaboration. The combined team of the Kornfelds and Majerus and the other faculty in their division trained numerous talented graduate students, postdoctoral fellows, and clinical fellows, many of whom are now in prominent positions throughout academia. Particularly remarkable was the large number of highly talented PhD and MD/PhD students who went through their labs. There was a time when the Hematology-Oncology Division at Washington University had more of these graduate students than the entire Biochemistry Department. Stuart was also the Director of the (MD/PhD) Medical Scientist Training Program at Wash U from 1991–1997 and later originated and still runs the Physician-Scientist Training Program there for research-track medical residents.

Stuart Kornfeld's life revolves around 5 aspects: family, sports, science, training, and service (Figure 4). Stuart is very family-oriented. There are not many fathers whose children have all moved back to the same city to be close to him, and two of them are even faculty members at Wash U today. In fact, Kathy, Kerry, and Carolyn are here today to felicitate their father. And Stuart also has the pleasure of watching his grandchildren grow up around him. When it comes to sports, Stuart was always a nat-

ural, becoming captain of his high school basketball and baseball teams. If you want to engage Stuart in a conversation on anything other than family, science, or academia, your best bet would be sports. One of his trainees (Hud Freeze) tells how, in 1982, he "bucked the biggest snow storm of the century to drive into St. Louis from San Diego, arriving at the lab after fighting immense snow drifts." Stuart's first typical taciturn words were apparently, "So...you made it...that's good." Then getting right down to business, Stuart got serious: "So...what do ya think Ozzie Smith will do for the Cardinals?" (future Hall of Famer Ozzie Smith had just been traded that week from the San Diego Padres to the Cardinals for hot-headed Cardinal Gary Templeton). According to Hud, Stuart added, "Ozzie's fast, Templeton's a problem" ...long smile... "I think they'll do all right." Stuart knew: Cardinals won the World Series that year. Stuart's current passion is now golf, and he is constantly working to stay in shape and improve his game.

Above and beyond his contributions to Washington University and the Division of Hematology-Oncology, Stuart has done yeoman service to science and academia (Table 2), including a stint as Associate Editor and then Editor of *Journal of Clinical Investigation*, and as Secretary, Councilor, and then President of the Association of American Physicians. In fact, one major reason we are here today at the Fairmont in Chicago was that Stuart was outgoing President of the AAP when I happened to be incoming ASCI President in 1998. Realizing that the traditional bicoastal Triple-Society meetings were failing,

we discussed the idea that the meeting should be moved to a more central location, a major airline hub, where everyone could fly out on Friday and return on Sunday. Our suggested choice was Chicago, and the organizing committee agreed, starting with the first meeting here at the Fairmont in April 1999.

Stuart lives and breathes science and has made major contributions to several fields including cell biology, glycobiology, and genetic diseases. With many great scientists, you can summarize their major achievements in a few short phrases or iconic images. And so it is with Stuart (see Figure 5). When I joined the lab in 1979, he had just published a classic series of papers working out the entire pathway for N-linked glycan chain processing (4), a scientific, technical, and intellectual tour de force that has since had a huge impact in many fields, basic and applied. Bucking the classic trend in showing detailed chemical structures, Stuart decided to summarize the findings using simple symbols to represent individual monosaccharides that made up the glycan chains (Figure 5, left panel). His idea caught on, and three decades later, this concept has expanded into a system of symbol nomenclature for monosaccharides that some of us updated in the primary textbook in the field (5) and is now used throughout the world (three of the eight editors are Kornfeld trainees). I was also fortunate to be in Stuart's lab and involved in his second classic set of studies, which eventually elucidated the entire mannose 6-phosphate pathway (refs. 6, 7, and Figure 5, right panel), by which newly synthesized lysosomal enzymes are selectively phosphorylated by a very novel mechanism and then specifically targeted

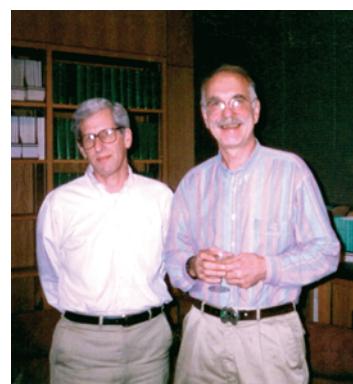


Figure 3
With Philip W. Majerus, 1995.

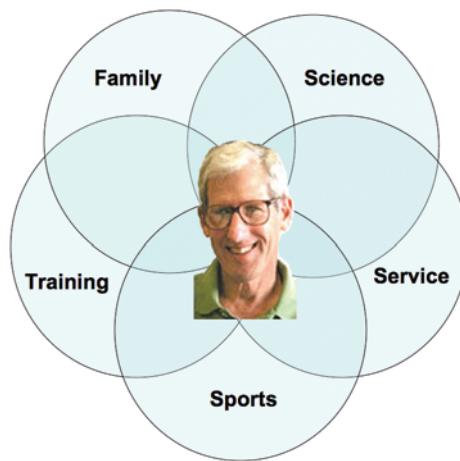


Figure 4
Major facets of Stuart Kornfeld's life and career.

to lysosomes, by mannose 6-phosphate receptors which he also isolated, cloned, and characterized (8). Since then Stuart has continued to make many major contributions in these and other fields, including subcellular trafficking and genetic diseases (9), and his work has now become part of figures in basic cell biology textbooks as well as in clinical journals. In fact, Stuart's glycan structures have now even made it into Hollywood movies (*Extraordinary Measures*, 2009) and are also featured in fashion jewelry used for fund-raising by the Congenital Disorders of Glycosylation Network (<http://www.cdgs.com/>). Needless to say, this network would not even exist today without Stuart's pioneering work, which paved the way for the discovery of these genetic disorders.

One measure of the success of a scientist is a legacy of trainees. I have already mentioned the joint mentoring provided by Stuart and Phil to Heme-Onc fellows, many of whom have gone on to prominent positions in academia. Stuart's own track record in this regard has been stellar, including 7 members of the AAP and 9 members of the ASCI. Of course, his wider impact arises from the many individuals whom his own trainees have mentored or trained. Stuart also had a unique and very effective style of leading his group. For a long time he did not even have regular lab meetings, preferring to interact directly with each individual on a regular basis. However, these interactions were partly based on how interesting your results were. Most of the time Stuart would just nod his head and perhaps make a brief remark to indicate his inter-

est or approval. But once in a great while, he got very excited and would run around the lab showing your results to everyone else. And when that happened, you knew that you had found something important. In fact as a trainee, you quite literally lived for the day when Stuart might actually do that. Another very unusual thing that Stuart did was to take on menial tasks in the lab to help important projects move along. I still remember the day when I had accumulated more than 50 different fractions of putative mannose-6-phosphorylated oligosaccharides that I had to individually desalt before I could even begin to analyze them. I was frankly quite depressed about having to do this huge, tiresome, and boring task. Stuart thought this was so important that

he actually took over the menial task of desalting of the samples and asked me to go ahead and analyze them – which I successfully did! You also had to be careful that Stuart did not take the opportunity to analyze your data before you got to it. As Marc Reitman put it, “Sometimes (usually for the most exciting experiments) I would take the printouts from the scintillation counter and go to the conference room (rather than to my desk in the lab) in order to plot and digest the data, so that I could interpret the results before Stuart did.” The combination of these types of inducements ensured that everyone in Stuart's lab performed at their very best and truly enjoyed the experience.

Finally, while the primary goal of this kind of presentation is to felicitate someone for a highly successful career, it is also an opportunity to poke some gentle fun and relate amusing anecdotes. However, what I thought would be a simple exercise proved to be remarkably difficult. Since I had no stories myself, I began first with Stuart's other trainees and then with the faculty and former faculty of Wash U, asking for amusing anecdotes about Stuart. Having failed there, I went on to ask his children. Even there I found it extremely difficult to find anything but perfection. In fact, to directly quote one of his children, “The truth is that there is no dirt on Dad – which in itself is one of his outstanding – and sometimes maddening – features! He really has no vices, no bad habits, no enemies. He has never done anything outrageous or questionable. He is generally extremely even tempered, with

Table 2
Service to academia beyond Washington University

1972–1975	Councillor, American Society for Clinical Investigation
1974–1977	Member, NIH Cell Biology Study Section
1976–1981	Editorial Board, <i>Journal of Biological Chemistry</i>
1977–1981	Associate Editor, <i>Journal of Clinical Investigation</i>
1981–1982	Editor, <i>Journal of Clinical Investigation</i>
1982–1987	Associate Editor, <i>Journal of Biological Chemistry</i>
1983–1987	Member, NIADDK Board of Scientific Counselors
1985–1991	Editorial Board, <i>Proceedings of the National Academy of Sciences</i>
1986–1994	Member, Scientific Review Board, HHMI
1986–1991	Secretary, Association of American Physicians
1988–1991	Editorial Board, <i>Journal of Cell Biology</i>
1991–1997	Councillor, Association of American Physicians
1992–2004	Editorial Board, <i>Molecular Biology of the Cell</i>
1995–2000	Medical Advisory Board, Howard Hughes Medical Institute
1997–1998	President, Association of American Physicians
1997–2007	Consulting Editor, <i>Journal of Clinical Investigation</i>
1998–Present	Albert Lasker Medical Research Awards Jury

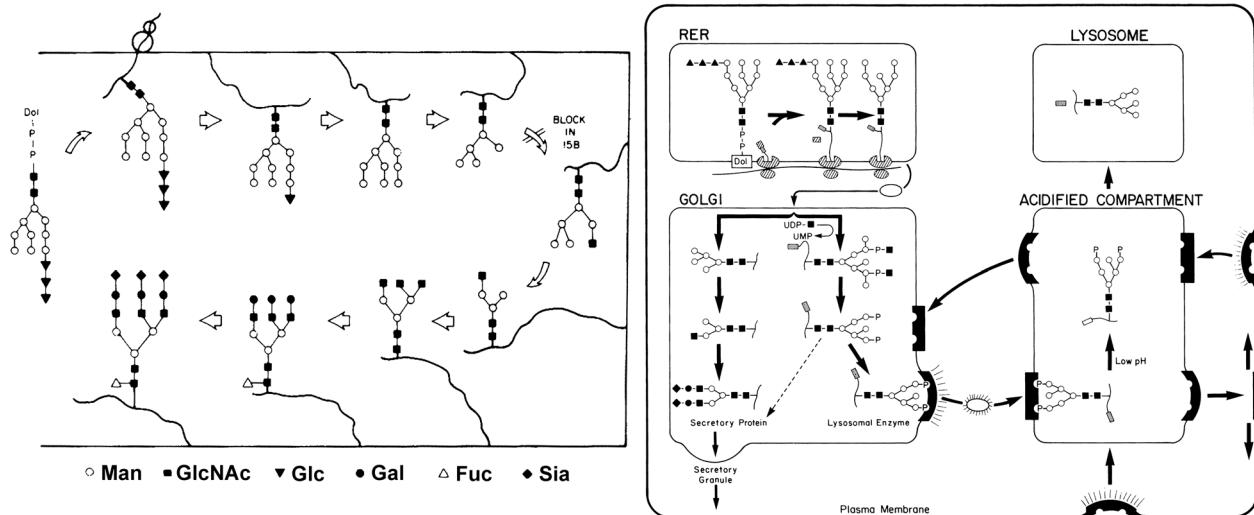


Figure 5

Processing and maturation of sialylated and phosphorylated N-glycans, as elucidated by the Kornfeld Lab. The left panel shows major steps in the biosynthesis, processing, and maturation of N-linked glycan chains (from ref. 4), and the right panel shows the selective phosphorylation of N-glycans on lysosomal enzymes, with mediates their selective targeting to lysosomes, via mannose 6-phosphate receptors (from ref. 7). Man, mannose; GlcNAc, N-acetylglucosamine; Glc, glucose; Gal, galactose; Fuc, fucose; Sia, sialic acid.

emotions ranging from mildly pleased to aggravated. If you prod him enough, he might admit that he isn't crazy about someone, but he would never show it. He is very fair and judicious. He is not prejudiced, but will evaluate people based on their abilities and actions. He's willing to give everyone a chance — however, they better take it! There is nothing worse than not doing your best at whatever your task is — be it sweeping the floor or designing an experiment. If someone does their best and has a good attitude, that will go far with him. Laziness is a terrible thing — as is whining and complaining. Dad is responsible and conscientious in the extreme — he isn't one to willy-nilly take on new things in a burst of enthusiasm, only to drop them later — once he decides that he's going to do something, it will be done — with a minimum of fuss and with no expectation of effusive thanks. And he is continually honing and improving and perfecting — his golf game being a perfect example. He never rests on his laurels!" I could not have said it better myself.

Even Stuart's alter-ego Phil Majerus could not come up with anything really unusual! Having failed at all these levels to find anything really amusing about Stuart, I finally spoke to his elder sister, Frances Goldstein (interestingly, Stuart is such a private man that I did not even know that he had an elder sister until very recently). Frances also had difficulty

remembering anything mischievous or unusual Stuart had done as a child, until she finally came up with one anecdote, which went as follows. Apparently during the Second World War, Stuart's uncle was in the army and used to send him various mementos. Stuart was inspired by the need for all Americans to work together in this just war and apparently formed a local unit of 8-year-olds, which, while they did not have an official name, were really Stuart's little army. Then one day, Stuart's uncle sent him a shovel, which had been used to dig foxholes out in the war front. Stuart took it upon himself to try out the shovel, and by the time his mother returned from being away for the day, she found that his little army had dug up the backyard with many foxholes! And knowing Stuart, I am sure that those foxholes were done to perfection!

I would like to close with a description of George Martin Kober, who lived from 1850 to 1931 and was AAP secretary from 1909 to 1917. It was said that "from . . . all accounts [he] . . . had great strength of character, loyalty both to persons and principles, together with humility and humanity of high degree" (10). I cannot think of a more apt description of Stuart Kornfeld, the gentleman physician-scientist and decent human being. His career has been characterized by absolute commitment to scientific truth and personal honesty, as well as complete disinterest in any of the self-promoting behavior regrettably so common these days, where people game the system to make themselves prominent in science. Stuart Kornfeld exemplifies the fact that unlike in many other fields, in science, nice guys do not finish last! Ladies and Gentlemen: please rise to applaud Stuart Kornfeld, the 2010 Kober Medalist of the Association of American Physicians!

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