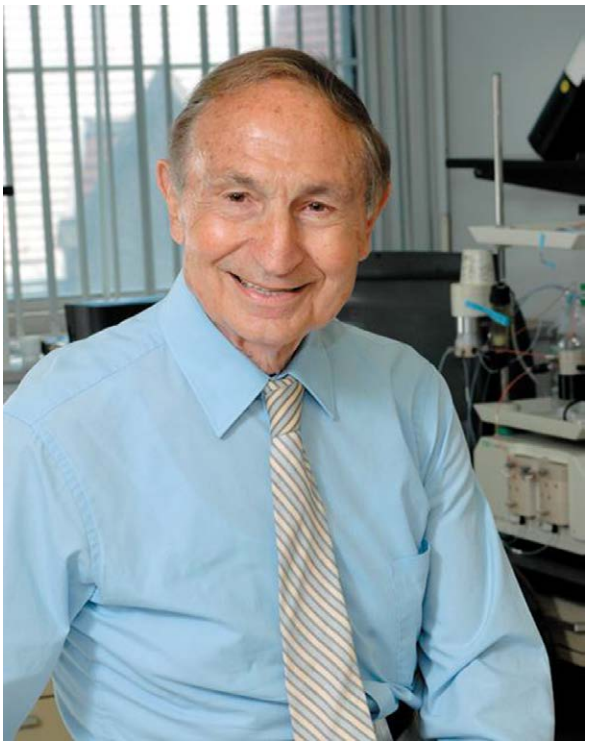
Angelo Scanu Memorial

Tribute to Angelo Scanu (1924–2018)

Celina Edelstein, Godfrey S. Getz, Santica M. Marcovina, John J. Albers, Marlys Koschinsky

Angelo Scanu spent almost the whole of his illustrious scientific career at the University of Chicago. Actually, he had 2 distinguished careers there: one devoted to plasma HDL (high-density lipoprotein) and the other to Lp(a) (lipoprotein(a)).

Angelo had come to the United States in 1955 on a Fulbright Scholarship, working with Irvine Page at the Cleveland Clinic and with Walter Hughes at the Brookhaven National Laboratories. It was at this time he began his pioneering work on lipoproteins, developing a delipidation procedure that yielded apolipoproteins in essentially a lipid-free state. This breakthrough opened up the field of apolipoprotein research. He came to the University of Chicago in 1961 to do his American internship in internal medicine—a second internship, having done the first one in Italy, where he had graduated cum laude from Sassari University Medical School in 1949. Angelo then joined the faculty in the Department of Medicine at the University of Chicago, where he remained until his retirement in 2011.



For the first 25 years of his research career, his focus was HDL, including the isolation and characterization of the structures of its 2 major apoproteins, A-I and A-II. Using innovative physicochemical methods, Angelo and his colleagues elucidated the role of the apolipoproteins in HDL structure. As a visiting investigator at CNRS (Centre National de la Recherche Scientifique), Gif-sur Yvette, France, he learned to apply small-angle X-ray scattering to the examination of lipoprotein structure. Along with Dr Vittorio Luzzati, these studies led to a series of important new findings on the structural organization of low-density lipoprotein and HDL. This venture highlighted Angelo's recognition of the importance of physical chemistry to the full understanding of lipoprotein structure—a view highlighted by his collaboration with Francois Kezdy, who was a close collaborator at the University of Chicago. Angelo was also a principal investigator in the Specialized Center of Research on Atherosclerosis where he studied the lipoproteins, low-density lipoprotein, and HDL of nonhuman primates.

In the mid 1980s, the focus of Angelo's laboratory shifted to the second theme of his research, Lp(a). In 1984, the group reported on the heterogeneity of Lp(a) particle size, which they correctly attributed to differently sized apo(a) (apolipoprotein(a)) moieties. In 1987, through a collaboration with Genentech, Inc, Angelo and his colleagues provided the first report of the unexpected similarity between the apo(a) component of Lp(a) and the fibrinolytic proenzyme plasminogen. The partial protein sequence data indicated the presence in apo(a) of domains corresponding to plasminogen kringle IV, kringle V, and protease sequences; the latter domain was shown to be inactive in apo(a). This work led to a publication in *Nature* in 1989, where Angelo's group showed that Lp(a) inhibits the binding of plasminogen to vascular cells—an important mechanism for the proposed antifibrinolytic effect of Lp(a). He and his collaborators were also the first group to report in 1989 the development of an ELISA method to measure Lp(a) that was insensitive to plasminogen and to report that on a weight basis, there was a difference in immunoreactivity of Lp(a) particles with different apo(a) isoforms. Equivalent reactivity was observed when protein concentration was expressed on molar basis and the article stressed the need for the development of appropriate standards to minimize the heterogeneity of Lp(a), which remains an area of focus in the field. The group also contributed a significant body of knowledge to our

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understanding of the structure and lysine-binding function of the critical apo(a) kringle IV type 10 domain during the 1990s.

One of the most significant contributions from Angelo's group was the key observation in 2003 that apo(a) contains covalently linked oxidized phospholipid. This observation underpins a key area of Lp(a) research at the present time, informing an exciting narrative that links this modification to a major proinflammatory role of Lp(a) in cardiovascular disease.

Angelo was one of the first clinicians to introduce a Lipid Clinic at the University of Chicago, which he led for >30 years until his retirement. There, he focused on treating patients with low HDL levels and high levels of Lp(a). Patients were attracted from many areas of the United States and from other parts of the world. He was the epitome of the clinician scientist. The impeccable quality of his bench science drew clinicians, surgeons, and pathologists to him. His professional colleagues recognized his many significant contributions with prestigious awards, including the Special Recognition Award of the Council on Arteriosclerosis and the George Lyman Duff Lecture.

Angelo was a devoted husband and father of 2 children, Gabriella and Marco, who enjoyed traveling with him and being exposed to his Italian heritage, tennis and his musical talents on the guitar. He also was proud of his 2 grandsons, one of whom has a natural talent for the classical guitar. He shall be missed greatly by his family, his many friends, and colleagues around the world.

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