Obituary

George J. Broze Jr., MD (2 August, 1946–19 June, 2019)

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George J. Broze Jr., MD

We were deeply saddened by the news that our mentor, colleague and friend George J. Broze Jr., MD, died of a heart attack on June 19, 2019. He was 72 years old. George was a luminary in the field of hemostasis and thrombosis research for close to 40 years.

Born in Seattle, George received his bachelor's degree in physics and medical degree from the University of Washington. His interest in blood coagulation began during his residency at North Carolina Memorial Hospital in Chapel Hill, where he had the good fortune to interact with Dr. Ken Brinkhous. In 1976 George moved to St. Louis to join the hematology division at Washington University as a clinical fellow. He would spend the next 43 years there, rising to professor of medicine and cell biology/physiology in 1991.

During his fellowship, George received a strong grounding in protein chemistry in the laboratory of Dr. Phil Majerus, working on vitamin K-dependent (VKD) coagulation proteins and particularly on factor VII. As an assistant professor in the early 1980s his laboratory purified human tissue factor (TF), and started investigating the regulation of the factor VIIa/TF complex. He began pursuing a finding reported by Peter Hjort in his 1957 doctoral dissertation indicating serum contained an activity that inhibited the procoagulant effect of TF. Subsequent studies, including insightful work from Dr. Sam Rappaport's group at the University of California San Diego, showed that this activity limited both factor IX and factor X activation and depended on factor Xa. Starting in 1987, a series of papers from George's laboratory described the isolation, cloning, and characterization of the inhibitor responsible for this effect, originally called lipoprotein-associated coagulation inhibitor (LACI), and subsequently TF pathway inhibitor (TFPI). Dr. Joe Miletich was a close collaborator during this formative time. Elucidation of TFPI's mechanism of action led to a reformulation of the original coagulation cascade that stressed the importance of factor VIIa/TF as the initiator of thrombin generation, and a "revised" model more compatible with the clinical syndromes caused by deficiencies of the various coagulation factors.

As with most paradigm shifts, the revised model of coagulation raised new questions. One involved the role of factor XI. As patients lacking factor XI have a mild bleeding diathesis, room had to be found for this protein in the new model. In the early 1990s, studies performed in George's laboratory and the laboratory of Dr. Kazuo Fujikawa at the University of Washington identified a novel mechanism for factor XI activation that fit the predictions of the model. As part of this effort, factor XI-deficient mice were generated in the Broze's laboratory. These animals, surprisingly, were strikingly resistant to thrombosis, an observation that has contributed to interest in developing therapeutic antithrombotics that target factor XI.

In addition to his pioneering work on TFPI and factor XI, George and his colleagues made other contributions that continue to expand and refine our understanding of how blood coagulation is regulated. His early work on an obscure VKD protein, protein Z, led to the discovery of the serpin protein Z-dependent protease inhibitor (ZPI). Studies on ZPI, along with work on TFPI, have provided key insights into the bleeding suffered by patients with hemophilia. George also contributed novel observations on thrombin-activatable fibrinolysis inhibitor and protein C that have implications for a range of pathologic processes, including thrombosis.

George's seminal contributions to science garnered important recognitions, including the Dameshek Prize from the American Society of Hematology, the Sol Sherry Prize from the American Heart Association, and the Pia Glas-Greenwalt Prize and a Distinguished Career Award from the International Society on Thrombosis and Haemostasis. These awards are well deserved; however, they are not why, or how, we remember George. He was not comfortable with accolades. George was a blue-collar scientist to the core, happiest in his own laboratory, fibrometer by his side. He seemed to take comfort from the sound of the clicking probe and the silence indicating the formation of a clot. He continued to work at the bench, seeking

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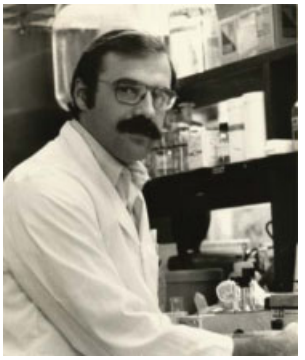
George J. Broze being bleed by Dave Gailiani (1992)



George J. Broze with a fibrometer (1982)

new insights firsthand, throughout his career. George was a collaborator, a competitor and, at times, a critic, but was always guided by the science. Those of us who had the good fortune to train under him appreciate that he was not only our mentor and a first-class scientist, but also our lab mate. He was always available for discussion. George had an incredible ability to identify important problems and to determine the proper way to investigate them. He taught us the right way to do science. We can think of no higher accolade.

In the end, tragically, it was a blood clot that silenced George. However, his scientific legacy will continue to speak volumes. We offer our deepest condolences to his wife Jilla, his sons George John "Yuri" Broze III and Charles "Chip" Broze Belpedio (Tony Belpedio), and his brother Greg Broze for their loss on behalf of former laboratory and clinical associates, colleagues and friends of George.