Obituary
Samuel Goldstein (1938–1994)

I always rejoice to hear of your still being employed in experimental researches into nature, and of the success you meet with. The rapid progress true science now makes, occasions my regretting sometimes that I was born too soon (Benjamin Franklin).

Sam Goldstein was one of those people who make such regrets heartfelt. As chronicled by his first publication in 1963 entitled "The Diagnosis of Old Age," to his most recent dozen publications dur-ing the past year, Sam tirelessly devoted his academic career to unravelling the intricacies of a process that is truly central to biology.

Sam was born and raised in Winnipeg, Manitoba where he received his M.D. and began his studies towards an understanding of the aging process. While undertaking his Residency training, and later as a Research Fellow in the laboratories of William Reddy, Mahlon Hoagland and John Littlefield at Harvard Medical School, Sam focused initially upon the relationship between diabetes and the premature onset of several features of aging. While still training in the Littlefield laboratory, Sam was quick to recognize the strengths of a newly developed experimental model that displayed what he referred to as "cellular epidemiology" and began experiments using the cultured human fibroblast model. Building upon and extending the seminal observations of Hayflick and Moorhead, that normal diploid fibroblasts had a finite replicative lifespan in culture, Sam began an extensive series of experiments spanning 25 years that helped to shape the field of experimental gerontology.

Soon after establishing his own laboratory at McMaster University in 1969, he examined the relationship between DNA repair and aging using fibroblasts from patients with DNA repair deficiencies, helped to establish the correlation between the maximum lifespan of a species and the replicative lifespan of their fibroblasts, and defined the contribution of mitotic, versus metabolic time to cellular aging. Sam's laboratory also published a number of studies testing the theoretically attractive idea proposed by Medvedev and Orgel in the earl '60s, that errors in the transcription and translation of gene products involved in DNA replication, mRNA transcription or translation, would result in self-amplifying errors, and an ensuing "error catastrophe". These studies culminated in a definitive demonstration that errors in protein synthesis do not increase during cellular aging.

Drawing from his knowledge of human genetics and metabolic disorders, Sam championed the use of fibroblasts derived from diabetics, from individuals predisposed to cancer, and from patients with the premature aging syndromes Progeria and Werner's as valid, manipulable experimental sys-

tems. In particular, his laboratory was instrumental in defining a set of genes that are overexpressed in Werner's syndrome fibroblasts undergoing premature replicative senescence. These recent studies are particularly exciting since some of the novel genes that were isolated appear to encode proteins capable of blocking cell growth, while others are implicated in age-related diseases such as osteoporosis diabetes mellitus and atherosclerosis. Quite fittingly, Sam has chronicled the recent evolution of research in cellular aging, to which he has contributed so significantly, in a succinct and objective review article of the field entitled "Replicative senescence: The human fibroblast comes of age" (*Science*, 249: 1129–1133, 1990). This review should be required reading for anyone interested in understanding this dynamic, but sometimes neglected, area of research within growth control.

Despite being recognized internationally as a leader in cellular gerontology, with the attendant heavy calls upon his time to speak at both public and scientific meetings and forums, Sam always had time for one of his favourite pursuits, the mental exercises associated with debating theoretical aspects of cellular mortality. During such conversations which many of us enjoyed, it became clear fairly quickly why Sam had devoted his scientific life to an area of research that, at times, has been viewed as unfashionable and less rigorous than other disciplines. He had a basic love of knowledge and a genuine interest in advancing this field that he, and others including those of us that were privileged to work with him, consider to be one of the "big" questions in Biology: what determines the mortality of cells, and by extension, of whole organisms?

To help answer this question, Sam not only created world class research laboratories, he was also an extremely effective teacher and lecturer. He exploited science, art, and humour creatively to communicate his knowledge in a fun and effective way. Thus, his seminars usually began with philosophical notes about an approach to science, or perhaps the relevance of test tube reactions to the global picture of aging. These notes would typically be illustrated with carefully selected slides from the humanities and end with a cartoon. Sam utilized these same skills, coupled with an uncommon sense of respect and fairness, in training his students and postdoctoral fellows.

Saying goodbye to a friend, respected colleague and former mentor is a duty that is impossible to relish, especially since Sam died without warning from a heart attack, at the height of his scientific productivity. Our regret is not that we were born too soon, but that Sam died so very prematurely. Both as a scientist and as a person, Sam will be dearly missed by many.

Karl Riabowol and Calvin Harley