Russell Ross 1929–1999

Russell Ross, a founder of contemporary vascular biology and a giant of atherosclerosis research, died in Seattle 18 March 1999 after a brief illness.

Born in Florida, Ross earned his PhD in 1962 at the University of Washington. For his thesis with Carl Benditt, he studied the biology of wound healing by using ultrastructural techniques to examine collagen production by mesenchymal cells.

At the outset of his career as an independent investigator, Ross recognized the key role of interactions between inflammatory leukocytes and mesenchymal cells in injured tissues, an enduring theme of his research. He recognized early on that a deeper understanding of the mechanisms underlying this problem would require a union of biochemical approaches with morphologic studies. Ross prized his dual appointments in both the Department of Pathology (which he eventually chaired for a dozen years) and the Department of Biochemistry in Seattle.

In the early 1970s, Ross made an important transition from his interest in wound healing in general to a particular focus on vascular cells. In a series of seminal papers, he systematically characterized cultures of arterial smooth muscle cells and studied the regulation of extracellular matrix proteins by these cells. He showed that arterial smooth muscle cells synthesized interstitial collagens, proteoglycans and elastin. With characteristic alacrity, Ross immediately appreciated the implications of this avenue of research for atherosclerosis. During the rest of his career, he united his interests in wound healing, inflammation and vascular cell biology to advance the field, and in so doing became a dominant figure in atherosclerosis.

Ross' 1974 discovery that platelets furnish a principal mitogen for smooth muscle cells in serum stimulated work around the world on this platelet-derived growth factor (PDGF). Ross followed his original observation in a determined and systematic fashion, always retaining broad biological perspective. The Ross laboratory reported the high-yield purification of this protein, characterized its receptors, and characterized the plurality of the potential cellular origins of this widespread and important mediator. His recent work with bone marrow chimeric mice with PDGF-deficient blood cells furnished important new proof of the involvement of PDGF in determining the composition of atherosclerotic lesions in mice.

Russell Ross' contributions, however, went well beyond a single molecule. His studies of the pathogenesis of atherosclerosis led him to the 'response to injury hypothesis of atherosclerosis'. Continued testing of this hypothesis has illuminated many aspects of the process of atherogenesis. Ross developed the key insight that atherosclerosis does not result from an inevitable degenerative process or simple accumulation of lipids within the artery wall. Instead, he viewed atherosclerosis as a fibroproliferative process that results from a specialized chronic inflammatory response, and demonstrated that arterial endothelium, mononuclear phagocytes, platelets and smooth muscle cells all elaborate growth-regulatory peptides that are important in intimal smooth muscle proliferation. Periodic authoritative reviews over the decades provided

updates to the response to injury hypothesis and revealed Ross' eagerness to revise his views in light of new data. The framework provided by these reviews stimulated work around the world and launched many careers devoted to unraveling the details of the model Ross strove constantly to perfect.

Ross was an extraordinarily gifted speaker and an enthusiastic and articulate advocate for his field. A frequent keynote speaker and named lecturer, he kept a daunting schedule, seemingly indefatigable even until the last weeks of his life. As a member of both the Institute of Medicine of the National Academy of Sciences and the American Academy of Arts and Sciences, he received many accolades for his accomplishments; the list of his awards and prizes is long.

He also shaped modern vascular biology through his trainees—many major figures passed through his laboratory. There is no doubt that his influence and inspiration drew many gifted young people into vascular biology and atherosclerosis research.

Russell embraced many facets of life with the same enthusiasm and energy he devoted to his scientific pursuits. A lifelong athlete, he would often skip lunch to run or lift weights. His frequent lectures and consulting roles for research programs around the world allowed him the opportunity to explore the art and music of many different cultures. Closer to home, his enthusiastic support of Seattle's music community led him to serve on the board of directors for the symphony. He also supported the Chamber Music Festival, and was especially proud of Seattle's new Symphony Hall—his tireless efforts as a board member helped propel its fruition. His beautiful home housed a contemporary art collection that featured not only the work of local sculptors and glass workers, but also the canvases of his wife and beloved companion Jean, a talented artist. Indeed, he often spoke with great pride of his wife and his children, Valerie and Douglas.

After stepping down as Chairman of the Department of Pathology in 1994, Russell Ross could have well been content to look back with satisfaction on his many accomplishments. Instead, he viewed his shedding of administrative burdens as an opportunity to plunge even more deeply into his scientific pursuits. He did some of his best work in the last few years, leading the charge to adopt mouse models to learn more about atherogenesis.

Although his dedication to the laboratory never flagged, Russell often spoke of the friendships he developed with colleagues over the years as one of the most enduring and gratifying aspects of the scientific enterprise. It would be hard to find a more loyal and devoted friend and mentor than Russell Ross, and he derived immense satisfaction from the collegiality of our profession. His many friends and colleagues, his close laboratory associates (including Elaine Raines) and especially his family are bereft by his passing. We shall not soon see another such champion of vascular biology and atherosclerosis research as Russell Ross, and we already miss him sorely.

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