Mitsuhiro Yokoyama, MD, PhD
1943–2016

Ken-ichi Hirata, MD, PhD

Dr. Yokoyama was a highly motivated researcher and scientist, and he made great contributions to cardiovascular research. He incorporated the technology of biochemistry, and molecular biology into his research to clarify underlying mechanisms in cardiovascular diseases. He expanded his research fields into endothelial function, oxidative stress and atherosclerosis by using cell biology, biochemistry and molecular biology. He clarified the mechanisms of endothelial dysfunction\(^5\,6\) and the role of oxidative stress in the process of atherosclerosis,\(^7\) and published numerous papers.

He developed endothelial cell-specific endothelial nitric oxide synthase (eNOS) transgenic mice\(^8\) and clarified the pathophysiological role of eNOS in cardiovascular diseases.\(^9\,10\) He also discovered that eNOS produces superoxide rather than NO through eNOS uncoupling in atherosclerosis.\(^11\)

Dr. Yokoyama was a hard worker, and a fair and sincere leader for young cardiologists and researchers. When the Great Hanshin-Awaji Earthquake with a magnitude of 7.2 occurred on January 17, 1995, and Kobe University Hospital and laboratories were severely damaged by the large-scale earthquake, he showed leadership in the reconstruction and recovery of Kobe University, and Kobe City. He taught us how a leader should behave.

As his final clinical research, Dr. Yokoyama and colleagues proposed that eicosapentaenoic acid (EPA) treatment with statin reduced cardiovascular events in Japanese hypercholesterolemic patients (JELIS study), and 18,645 patients were recruited. It was found that EPA treatment did reduce cardiovascular events and Dr. Yokoyama presented the results at the late-breaking clinical trials of the AHA Annual Meeting at Dallas, Texas, USA in 2005. The results were also reported in \textit{The Lancet},\(^12\) and the JELIS study was recognized as the pioneer of large-scale clinical trials in Japan.
He was an outstanding researcher, clinician, and teacher. After his retirement from Kobe University, he served as Principal of the Hyogo Awaji Prefectural Hospital from 2011 to 2013, and then Principal and advisor at the Himeji Cardiovascular Center from 2013 to 2016. Even after retiring from Kobe University, he continued his passion for clinical research and education, and taught the importance of research thinking for young doctors. He always encouraged young doctors to “Strike while the iron is hot.” We learned a lot about the fun and excitement of science. Dr. Yokoyama will be remembered and beloved by his family, friends and colleagues.

References