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## Editorial: Claude Klee, Sten Orrenius and Katsuhiko Mikoshiba



This special issue is dedicated to Prof. Ernesto Carafoli on the occasion of his retirement as Editor in Chief of BBRC. Prof. Carafoli was recruited to the BBRC Editorial board during the late 1970s by Jean Pierre Ebel. Since then not only has he brought an exceptionally broad expertise that encompasses biochemistry, molecular and structural biology, biophysics, and medicine, as illustrated in the following summary of his scientific achievements, but also a tenacious, unflagging commitment to insure and promote the publication of high quality, state of the art manuscripts in BBRC. His devoted service to the journal resulted in his promotion as Editor in Chief in January of 2013, as the successor of Dr. Bill Lennarz.

Early in his career Ernesto Carafoli was at the forefront of the biochemistry of ion transport and bioenergetics. His now classical studies, initiated in Dr. Albert Lehninger's laboratory, established the existence of different pathways for the uptake and release of calcium from mitochondria. This early interest in mitochondrial function led to his later work on calcium transport in the plasma membranes and endoplasmic reticulum, making him one of the world's experts in this area. He has made fundamental contributions to the purification and characterization of the many isoforms of the plasma membrane calcium ATPases and the reconstitution of the calcium pumps associated with these enzymes. Human plasma membrane  $\text{Ca}^{2+}$ -ATPases were cloned in his laboratory and the deduced sequences of these enzymes enabled him to localize the calmodulin-binding domain he had previously identified and characterized. The determination of the sequences of these enzymes, a major achievement, provided him with the unique opportunity to establish the molecular basis for the mechanism of action and the regulation of this important enzyme. He then extended his research to the study of calmodulin, the universal mediator of calcium signaling acting as a second messenger. He demonstrated the presence of calmodulin-regulated enzymes in the nucleus and unlocked a new chapter in the regulation of cellular processes by calcium.

Following his retirement from the Swiss Federal Institute of Technology (ETH) in Zurich, he joined the University of Padova and founded a new research institute, the Venetian Institute of Molecular Medicine, where a group of leading scientists from around the world could pursue a variety of excellent research programs. He served as Scientific Director of this institute for the first five years during which he continued to spearhead a highly successful new scientific research with collaborators from all over the world. The first project focused on the regulation of the endoplasmic reticulum  $\text{Ca}^{2+}$ -ATPase, SERCA, by phospholamban. The chemical synthesis of phospholamban, the determination of its solution structure by nuclear magnetic resonance followed by the identification of the SERCA binding-site for phospholamban were major steps toward understanding the regulation of this key enzyme in calcium transport. Extending his early work on the proteolysis of the sodium/calcium exchanger by the calcium-dependent protease, calpain, in collaboration with Prof. Nicotera, UK (now in Germany), he revealed a novel role of this exchanger in neuronal degeneration. The modulation of the sensitivity of neurons to calcium is also the subject of another collaborative project with Prof. Naranjo, Spain, dealing with the regulation of transcription of calcium transporters by the calcium-regulated transcription factor, DREAM. Equally impressive is his recent identification of mutations in the plasma membrane  $\text{Ca}^{2+}$  pump responsible for hereditary diseases and the understanding of the role of these mutations in the pathogenesis of deafness in collaboration with Dr. Fabio Mammano.

To honor Professor Carafoli, this Special Issue comprises contributors that reflect on the broad range of his calcium signaling research interests. He will be particularly thrilled to note that many of the present world leaders in the field were his students, and post-doctoral fellows and other his collaborators.

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