IJAE
Vol. 116, n. 1 (Supplement): 89, 2011
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

The mechanism of injury-induced [Ca2+]i oscillations in the endothelium of excised rat aorta

Germano Guerra[1], Franco Tanzi[2], Roberto Berra Romani[3], Abdul Raqeeb[4], Julián Torres-Jácome[5], Francesco Moccia[2]

[1] Dipartimento di Scienze per la Salute, Università degli Studi del Molise, Campobasso, Italia
[2] Dipartimento di Fisiologia, Università degli Studi di Pavia, Italia
[3] School of Medicine, Department of Biomedicine, Benemérita Universidad Autónoma de Puebla, México
[4] Department of Pharmacology and Therapeutics, Faculty of Medicine, University of Calgary, Canada
[5] Instituto de Fisiología, Benemérita Universidad Autónoma de Puebla, México.

Endothelial injury is the primary event that leads to a variety of severe vascular disorders. The signal transduction pathway which drives the subsequent healing process is far from being fully elucidated. Mechanical injury elicits a Ca2+ response in the endothelium of intact rat aorta, which comprises an initial Ca2+ release from inositol-1,4,5-trisphosphate-sensitive (IP3Rs) stores followed by a long-lasting decay phase due to Ca2+ entry through uncoupled connexons. In a minor fraction of cells, the Ca2+ signal adopts an oscillatory pattern whose molecular underpinnings are yet to be elucidated. In the light of the role played by repetitive Ca2+ spikes in regulating tissue regeneration, the present study aims at elucidating the mechanisms underlying injury-induced Ca2+ oscillations. The repetitive Ca2+ signal reversibly ceased upon removal of extracellular Ca2+ or addition of the inorganic cations, La3+ and Ni2+. Moreover, the spiking response was abolished by the gap-junction blockers, heptanol and 18 beta-glycyrrhetinic acid and by interfering with the Ca2+ entry-mode mode of the Na+/Ca2+ exchanger (NCX). The InsP3-producing agonist, ATP, resumed Ca2+ oscillations in silent cells, while the phospholipase C inhibitor, U73122, inhibited the oscillatory signal. The latter was also prevented by the SERCA inhibitors, thapsigargin and cyclopiazonic acid acid. These data show that injury-induced [Ca2+]i oscillations require the coordinated interplay between NCX-mediated Ca2+ entry and InsP3-dependent Ca2+ release. Besides directly gating Ca2+ inflow, uncoupled connexons might let Na+ into the cells and stimulate Ca2+ entry through NCX by increasing submembranal Na+ levels.

Keywords: rat aorta, endothelial injury, Ca2+ oscillations, gap junction blockers, Na+–Ca2+ exchanger, InsP3 receptors