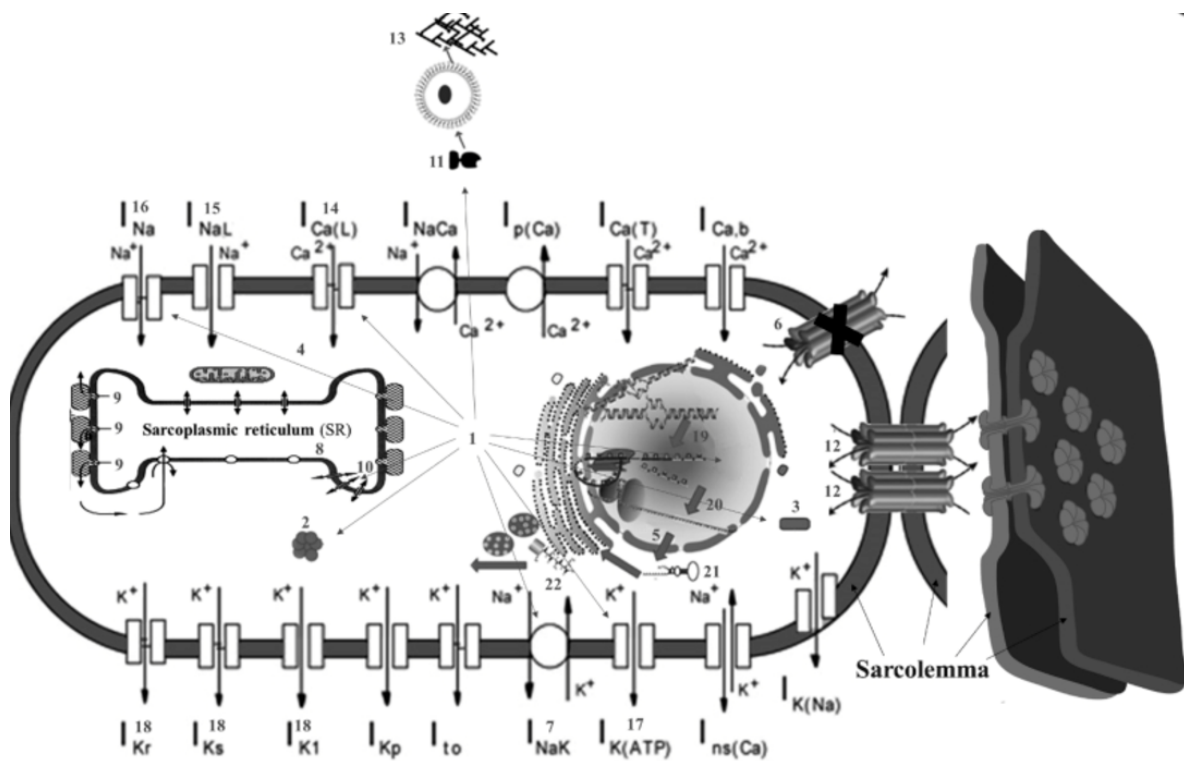


Cardiomiopatia atrial - 2017

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Parabéns ao querido Javier e amigos por contribuir com a assim denominada cardiomiopatia atrial. Nos recentemente publicamos um manuscrito que aborda as causas intrínsecas da fibrose nos átrios. (Pérez-Riera AR, de Abreu LC, Barbosa-Barros R, Grindler J, Fernandes-Cardoso A, Baranchuk A. P-wave dispersion: an update. *Indian Pacing Electrophysiol J.* 2016 Jul - Aug;16(4):126-133.) Mostramos o complicado jogo deste fenômeno pró-arritmogênico da fibrose que em última instancia tem por origem 22 pontos de modificação celular expressado na figura abaixo.

O full text está disponível no Pubmed.



Main action in 22 points of cardiac cell

- 1) Excess of reactive oxygen species (ROS);
- 2) CaMKII activation or Ca²⁺/calmodulin-dependent protein kinases II;

- 3) c-Src activation (SRC proto-oncogene, non-receptor tyrosine kinase);
- 4) PKC (Protein kinase C) enzymes play important roles in several signal transduction cascades. Abnormal splicing, activation of CaMKII, c-Src, and PKC are among emerging new antiarrhythmic;
- 5) mRNA of Na⁺ current;
- 6) Impair gap junction CX43 conduction resulting in reduced myocyte coupling;
- 7) NCX: Na⁺/Ca²⁺ exchanger. The NCX removes a single Ca²⁺ ion in exchange for the import of three Na⁺ ions. It is considered one of the most important cellular mechanisms for removing Ca²⁺;
- 8) Phospholamban (PLB): It is a 52-amino acid integral membrane protein that regulates the Ca²⁺ pump in cardiac muscle and skeletal muscle cells;
- 9) Ryanodine receptor (RyR) participates in different signaling pathways involving Ca²⁺ release from intracellular organelles. It is the major cellular mediator of Ca²⁺ induced Ca²⁺ release (CICR) in animal cells. RyR2 is primarily expressed in myocardium;
- 10) Sarco-/endoplasmic reticulum Ca²⁺-ATPase (SERCA) resides in the sarcoplasmic reticulum (SR) within myocytes. It is a Ca²⁺ ATPase that transfers Ca²⁺ from the cytosol of the cell to the lumen of the SR at the expense of ATP hydrolysis during muscle relaxation;
- 11) Transforming Growth Factor- β (TGF- β) leads to the activation of different downstream substrates and regulatory proteins, inducing transcription of different target genes that function in differentiation, chemotaxis, proliferation, and activation of many immune cells;
- 12) Zonula Occludens-1 (ZO-1) or tight junction protein. It is located on a cytoplasmic membrane surface of intercellular tight junctions. The encoded protein may be involved in signal transduction at cell–cell junctions;
- 13) Extracellular fibroblasts activation and collagen deposition;
- 14) Increase in L-type Ca²⁺ current;
- 15) Increase in late Na⁺ current. Selective inhibition of cardiac late I_{Na} with eleclazine confers dual protection against vulnerability to ischemia-induced AF and reduces atrial and ventricular repolarization abnormalities before and during adrenergic stimulation without negative inotropic effects.
- 16) Na⁺ current reduction;
- 17) ATP-sensitive K⁺ channel (KATP channel) inhibition;
- 18) I_{to}, I_{Ks} and I_{Kr} inhibition;

19) Transcription;

20) Splicing;

21) microRNA;

22) Translation.