Atrial fibrosis cellular mechanism

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Parabéns ao querido Javier García Niebla e amigos por contribuir com a assim denominada cardiomiopatia atrial[1]. Nos recentemente publicamos um manuscrito que aborda as causas intrínsecas da fibrose nos átrios[2]. 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 disponivel no Pubmed.

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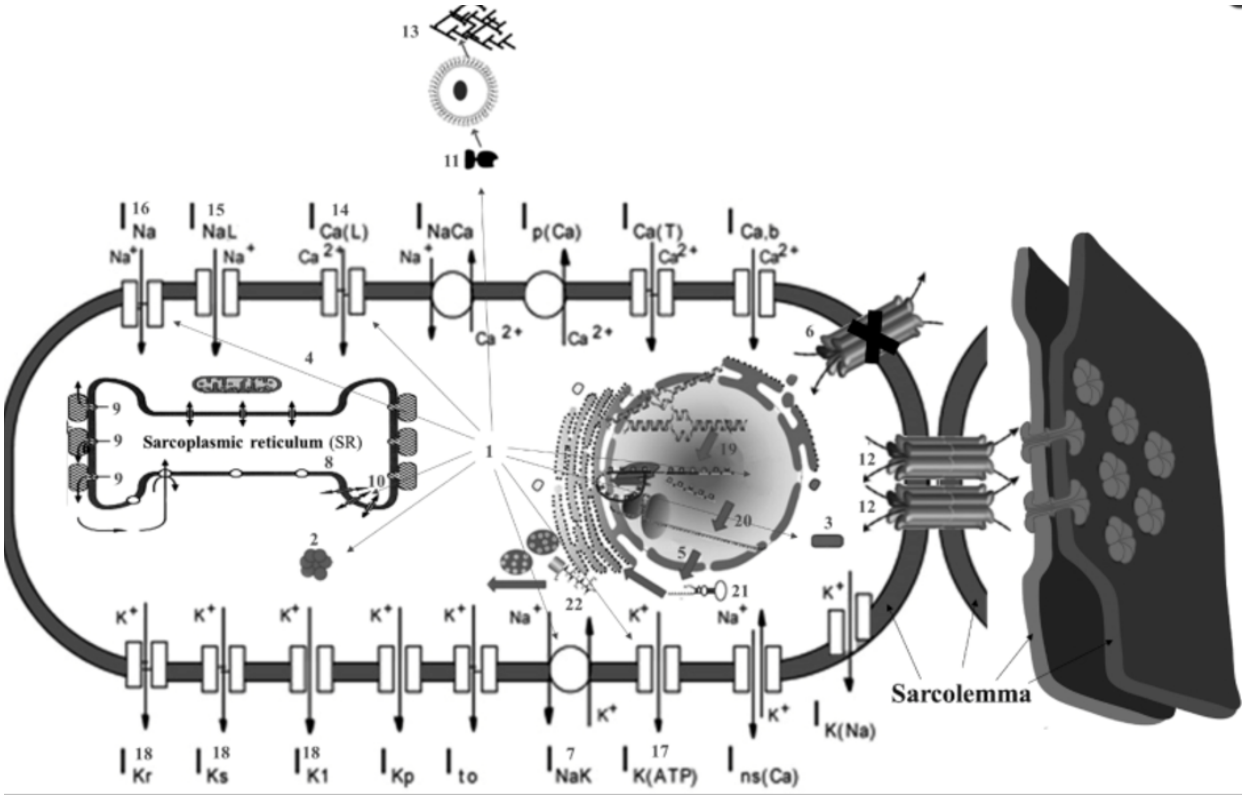
[1] Lacalzada-Almeida J, García-Niebla J. How to detect atrial fibrosis. J Geriatr Cardiol. 2017 Mar;14(3):185-194. doi: 10.11909/j.issn.1671-5411.2017.03.008.

[2] 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



Main action in 22 points of cardiac cell

1) Excess of reactive oxygen species (ROS);
2) CaMKII activation or Ca^{2+}/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^+/Ca^{2+} exchanger. The NCX removes a single Ca^{2+} ion in exchange for the import of three Na^+ ions. It is considered one of the most important cellular mechanisms for removing Ca^{2+};
8) Phospholamban (PLB): It is a 52-amino acid integral membrane protein that regulates the Ca^{2+} pump in cardiac muscle and skeletal muscle cells;
9) Ryanodine receptor (RyR) participates in different signaling pathways involving Ca^{2+} release from intracellular organelles. It is the major cellular mediator of Ca^{2+} induced Ca^{2+} release (CICR) in animal cells. RyR2 is primarily expressed in myocardium;

10) Sarco-/endoplasmic reticulum Ca^{2+}-ATPase (SERCA) resides in the sarcoplasmic reticulum (SR) within myocytes. It is a Ca^{2+} ATPase that transfers Ca^{2+} 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 Ca^{2+} 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.