

Expression pattern of Anoctamin (Ano) family in heart and role of Ano1 in ischemia-induced arrhythmia

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Calcium-activated chloride channels (CaCCs) play a fundamental role in many physiological processes including regulation of cardiac excitability. However, the molecular identity of CaCCs remained unclear until Yang *et al.* revealed that Anoctamin 1 (Ano1) is a candidate CaCC [Yang *et al.* (2008) *Nature* 455, 1210-1215]. We hypothesized that activation of Ano1 contributes to ischemia-induced arrhythmia by shortening action potential duration (APD). To test this hypothesis, we established an infarction model in mice to induce arrhythmia. Quantitative real-time RTPCR and western blot were used to examine the expression pattern and level of Anoctamin family. Our results indicate that expression pattern of Anos was not altered by ischemia, while Ano1 and Ano6 were strongly up regulated in the ischemic group. We then acutely isolated cardiac myocytes to perform whole-cell patch recording with respect to the biophysical properties and pharmacological profile of CaCC. We found a Ca²⁺-activated chloride current with an anion selectivity sequence of SCN⁻ > I⁻ > Cl⁻ > Glut in both normal and ischemic cardio myocytes. The density of this current is dependent upon intracellular [Ca²⁺]. This current exerts outward rectification and voltage-dependent relaxation and it can be blocked by external niflumic acid. Interestingly, the density of this Ca²⁺-activated chloride current was increased significantly in cardio myocytes isolated from infarction hearts compared to that from normal hearts. Furthermore, APD was shortened significantly in ischemic cardiomyocytes compared to normal ones. Taken together, our results indicate that activation of CaCC (most likely Ano1) contributes to ischemia-induced arrhythmia by shortening APD.

Biography

Dr. Zhi-Ren Zhang has completed his M.D. from Harbin Medical University (HMU), P. R. China and he then received his Ph.D from Semmelweis University, Hungary and postdoctoral studies from the Department of Physiology, Emory University School of Medicine. He is the Director, Institute of Clinical Pharmacy and Pharmacology of HMU and the co-Chair of Department of Cardiology, the 2nd Affiliated Hospital of HMU. He has published more than 30 original research papers in reputed journals and two peer reviewed book chapters and two peer reviewed review articles.