Investigating the role of plasma membrane calcium ATPase subtype 4 (PMCA4) in cardiac electrical activity

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Heart failure (HF) confers a poor prognosis with an annual 30-40% mortality rate for patients. 40% of HF-related mortality is linked to a sudden arrhythmic event. Increased intracellular calcium has been observed in failing cardiomyocytes, and attention has been drawn to calcium handling and cardiac electrical activity in these cells. Plasma membrane calcium ATPases (PMCA), a family of calcium-extrusion pumps, were found to contribute little to total calcium-extrusion processes in normal cardiomyocytes but can be activated by Ca^2+ -dependent processes. We have previously shown that PMCA4 is part of a protein complex which modulates localised Ca^2+ levels in cardiomyocytes. We have found that genetic ablation of PMCA4 (PMCA4KO) protected against hypertrophy-induced HF in mice. However, little is known about how PMCA4 may influence arrhythmic events. Therefore, we sought to assess PMCA4s role in cardiac electrical signalling. We report that no significant difference was found in any ECG parameters between PMCA4KO and PMCA4 wild-type mice in either conscious or unconscious ECG. No significant difference was found in gene expression of calcium handling proteins. However, in PMCA4KO mice, a trend was seen for reduced expression of potassium channels, including KIR2.1 (inward-rectifier channel encoded by KCNJ2), Kv1.4 and Kv4.2 (transient-outward channels encoded by KCNA4 and KCND2 respectively). Such channels have important roles in cardiac repolarisation, which governs the action potential duration. This study, so far, has found no significant difference in cardiac electrical activity between PMCA4KO and PMCA4 wild-type mice under basal conditions. Further assessment under arrhythmic stress and hypertrophic conditions is required.

Biography

Mohamed Elsakka was awarded half a scholarship, free of charge grant, by Mansoura University due to his good performance in high school. He has gained his Bachelor of Medicine and Surgery (MBBCh Degree) from Mansoura-Manchester Programme for Medical Education, Mansoura University, Egypt, with excellent degree with honour, and he was one of the top five students of his class. Afterwards, he started working as a Cardiothoracic resident at Mansoura University Hospitals. He is fully registered with the GMC, and has applied for his Master's Degree in Cardiovascular research at the University of Manchester under supervision of Dr. Elizabeth Cartwright.

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