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EDITORIAL

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Telocytes: Supporting cells participating in ventricular arrhythmogenesis?

In the article published in the Journal of Arrhythmia,[1] DeSimone et al identified distinctive cell population in canine ventricles through immunostaining of Anoctamin-1 (ANO-1, a Ca^{2+}-activated Cl^- channel) and Kit (a receptor tyrosine kinase). Under this setting, they found (a) the cells with ANO-1 (+), Kit (+), having the picture of telocyte-gastrointestinal interstitial cells of Cajal as in epicardium, subepicardium, and mid-myocardium (but not endocardium), (b) the cells with ANO-1 (+), Kit (−), appearing in the morphology similar to cardiac myocytes in myocardium (but no epicardium), (c) cells with ANO-1 (−), Kit (+), most likely representing cardiac mast cells (very rare), and most ventricular myocytes with ANO-1 (−), Kit (−).

Telocytes, previously referred to as interstitial Cajal-like cells and featured by their extremely long cellular prolongations, are accepted as a distinct type of interstitial cells in heart.[2] Interstitial cells of Cajal, the mesoderm-derived mesenchymal cells found in the early 1970s, control the gastrointestinal motility through generating pacemaker potentials. The interstitial cells of Cajal achieve a 3D network because of their extensive telopodes, not only support cardiac stem cells but also play a major role in tissue engineering.[2] Telocytes identified by Kit (+) were found in the thick muscular sleeve of pulmonary veins, particularly in the patients with atrial fibrillation.[3] These findings suggested the possibility that telocytes may contribute to the arrhythmogenesis of pulmonary veins, although the mechanisms remained unclear.

There are several Cl^- currents identified in cardiomyocytes, which play an important role in the pathogenesis of ventricular or atrial arrhythmia.[4] The Ca^{2+}-activated Cl^- current comprises one of the major anion currents that modify cardiac electrical activity and induce arrhythmogenesis. Through immunostaining for ANO-1, DeSimone et al, provided the potential link of telocytes and ventricular electrical activity.[1] They speculated that Ca^{2+}-activated Cl^- channel in telocytes may result in the occurrence of delayed afterdepolarizations and shortening of action potential duration, thus ANO-1 (+) cells carry the arrhythmogenetic potential through enhancing triggered activity or genesis of reentrant circuits. The previous animal study suggested that ischemia induced increasing cardiac ANO-1 expression and may be responsible for, at least in part, ischemia-induced arrhythmias.[5] Moreover, this study identified the presence of Ca^{2+}-activated Cl^- channel in some particular populations of ventricular myocytes. This finding confirms the heterogeneity of Ca^{2+}-activated Cl^- channel expressions in cardiomyocytes, which enhances ventricular arrhythmogenesis through regional electrical inhomogeneity.

However, the Ca^{2+}-activated Cl^- channel detected in this study was based on immunolabeling,[1] it was difficult to assess the current density through ANO-1 staining. Further investigations are warranted for appreciation of the exact mechanisms how telocytes are involved in ventricular arrhythmogenesis such as the cross talk between telocytes and other ventricular cells, and the contribution of telocytes in ventricular structural or electrical remodeling. It may be helpful in delineating the role of telocytes in ventricular arrhythmia from the studies on Kit and/or ANO-1 knockdown animals (especially in the pathological setting of heart failure or myocardial ischemia) or ANO-1 blockers (eg, niflumic acid, T16Ainh-A01).

This study explored the distinctive cell population in the canine ventricles and provided novel insight into ventricular arrhythmogenesis. It is a big challenge to more fully understand the regulation of cardiac electrical activity from different populations of ventricular cells. Targeting distinctive cells or ionic profiles will be expected to lead to new therapeutic strategy for arrhythmia.

CONFLICT OF INTEREST

Authors declare no conflict of interests for this article.

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