Defining the Complexity of the Junctional Membrane Complex

Barry London

Each heart beat in every cardiac myocyte begins with the surface membrane depolarization during an action potential that opens L-type Ca\(^{2+}\) channels and allows the influx of a small amount of extracellular Ca\(^{2+}\) that triggers a larger release of Ca\(^{2+}\) from the intracellular store, the sarcoplasmic reticulum (SR), through ryanodine receptors (RyR2).\(^1,2\) This process, known as Ca\(^{2+}\)-induced Ca\(^{2+}\)-release, is the primary mechanism underlying excitation–contraction coupling in the heart. Cardiac myocytes are relatively large cells, and efficient cardiac function requires not only the rapid sequential activation of contraction between cells but also the simultaneous activation of the contractile apparatus within each cell. To accomplish this, adult cardiac myocytes localize L-type Ca\(^{2+}\) channels in deep membrane invaginations known as transverse tubules (T-tubules), located along the Z-lines adjacent to the SR Ca\(^{2+}\) release channels in highly ordered structures known as dyads. The potential importance of these organized junctional membrane complexes has been defined during the last decade using in situ imaging techniques that show their loss in pathological conditions, including myocardial infarction and heart failure.\(^3\)

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Additional proteins essential for the structure and function of the junctional membrane complex have been identified. Junctophilin-2 (JPH2) connects the T-tubular and SR membranes and is downregulated in many models of heart failure.\(^4–6\) Of greater note, JPH2 disruption leads to heart failure.\(^7,9\) Do polymorphisms in SPEG predispose to heart failure?\(^8\) The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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failure and arrhythmias? Do mutations in SPEG cause inherited forms of sudden death?

Although SPEG was the only new protein identified by the MS/MS screen using JPH2 and RyR2, it is likely that other unidentified proteins are playing a role in the junctional membrane complex. These proteins may bind to either JPH2 or RyR2. Alternately, future studies could now use SPEG as bait to identify other members of the protein complex. During the past several years, our understanding of the junctional membrane complex has increased. The article of Quick et al\textsuperscript{12} has contributed to our improved understanding. That said, we do not yet know just how complex the junctional membrane will turn out to be.

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None.

References

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