Myocyte Ultrastructure: Clusters of L-type Ca channels

Key Triad Proteins

Organization of cardiac and skeletal ryanodine receptor (RyR) arrays
Calcium-Induced Calcium Release

Figure 5A. The Ca current dependence of shortening in guinea-pig ventricular myocyte (A) and of Ca transient amplitude (B) in rat ventricular myocyte. Conditioning pulses were applied to study the effect of Ca current on different ICa. The Ca transient amplitude at the end of each pulse was used to determine the ICa. If SR Ca release was Ca2+-dependent, the ICa would produce a greater contraction at peak Ca2+ as a more positive peak potential. The lack of such effects during the Ca current (ICa) dependence of the transient amplitude indicates that there is no apparent Ca2+-dependence of the Ca current (ICa) on the Ca transient amplitude. The data in the two experiments indicated a small difference in peak current (ICa) from unpublished experiments of D.M. Bell, J.E.B. Bridge & R.W. Stoker and B. Fromm-Cornell et al., 1987.

Constellation of Ca^{2+} release units (CRUs) in cardiac myocytes

Calcium Sparks

Calcium sparks: A: Two-dimensional confocal images of Ca2+ sparks in a quiescent cardiac myocyte (scan rate 1.0 s/frame). B: Line-scan confocal images of an action potential (AP)-elicited [Ca2+]-transient (top) and a spontaneous spark (bottom) (scan rate 2.0 ms/line). Time and space ordinates are displayed in the horizontal and vertical directions, respectively.
Depolarization-evoked Ca²⁺ sparks. Under conditions of whole cell patch clamp and intracellular dialysis of the indicator fluo 3, a small depolarization (from −50 mV holding potential to −40 mV) evoked Ca²⁺ sparks randomly in space and time. Summation of these discrete, brief, and localized events determines the time course and magnitude of the global [Ca²⁺]i signal (bottom). Scale bar: 10 µm.

Calcium blinks

Local Control of Excitation-Contraction Coupling
**Ventricular Action Potential**

<table>
<thead>
<tr>
<th>Current</th>
<th>Probable clone</th>
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</thead>
<tbody>
<tr>
<td>$\mathbf{i}_{\text{Na}}$</td>
<td>SCN5A</td>
</tr>
<tr>
<td>$\mathbf{i}_{\text{CaL}}$</td>
<td>DMP receptor</td>
</tr>
<tr>
<td>$\mathbf{i}_{\text{Na/Ca}}$</td>
<td>NCX</td>
</tr>
<tr>
<td>$\mathbf{i}_{\text{K_1}}$</td>
<td>Kir2.1x</td>
</tr>
<tr>
<td>$\mathbf{i}_{\text{K_3}}$</td>
<td>Kv4.3x</td>
</tr>
<tr>
<td>$\mathbf{i}_{\text{K_2}}$</td>
<td>HERG</td>
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<tr>
<td>$\mathbf{i}_{\text{K_0}}$</td>
<td>KcLQ10/minK</td>
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</tbody>
</table>

Adapted from G. Marban & Cardiovasc Res 1998

**Movements of Calcium in Excitation-Contraction Coupling in Cardiac Muscle**

Adapted from Figure 23-5, Berne & Levy
Regional Heterogeneity

Rogue RyRs underlie sparkless release: a hypothesis

Three Main Transporters of Ca2+ from Cytosol
Sarcoplasmic Reticulum Function

A. Diastolic Ca Leak

B. Systolic Ca Release

SR Ca content dependence of SR Ca leak and release during EC-coupling

NCX function during ventricular AP
Sarcoplasmic Reticulum Function

A. Control
B. Caffeine

Calcium Fluxes

A. 
B. 
C. 
D. 

Post-Rest Potentiation

A. 
B. 
C. 
D. 
E. 
F. 
G. 
H. 
I. 
J. 
K. 
L. 
M. 
N. 
O. 
P. 
Q. 
R. 
S. 
T. 
U. 
V. 
W. 
X. 
Y. 
Z. 

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Effects of Duration of Depolarization

Figure 47. The duration of depolarization determines the direction of the contractile "response" in a guinea-pig ventricular myocyte. Membrane potential ($V_m$) and external step (ES) is in a period of resting cell length under voltage-clamp (37°C, 45mM NaCl). (From Lembo & Grønn-Larsen, 1989, with permission.)

Effects of Stimulus Frequency

Figure 48. Effect of a transient increase in frequency (from 0.1 to 1.5 Hz) on twitch force in rabbit ventricular muscle (37°C).

Force-Frequency Relation

Figure 49. Effect of frequency (from 0.1 to 2 Hz) on twitch force in rabbit (circles), rat (squares) and guinea-pig ventricular muscle (triangles). Data for rabbit and rat are at 37°C. Data for guinea-pig are at 36.5°C and were taken from Kishino & Taka (1985). RCCP were initiated within 5 sec of the last steady state contraction.
Intermolecular relationships between LCCs and RyRs in normal and diseased heart cells

Arrhythmogenesis

Proprietary for triggered arrhythmias

Ventricular myocyte