Cardiac conduction

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15/01/2022
Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references


Reactome database release: 78

This document contains 8 pathways (see Table of Contents)
Cardiac conduction

Stable identifier: R-HSA-5576891

The normal sequence of contraction of atria and ventricles of the heart require activation of groups of cardiac cells. The mechanism must elicit rapid changes in heart rate and respond to changes in autonomic tone. The cardiac action potential controls these functions. Action potentials are generated by the movement of ions through transmembrane ion channels in cardiac cells. Like skeletal myocytes (and axons), in the resting state, a given cardiac myocyte has a negative membrane potential. In both muscle types, after a delay (the absolute refractory period), K+ channels reopen and the resulting flow of K+ out of the cell causes repolarisation. The voltage-gated Ca2+ channels on the cardiac sarcolemma membrane are generally triggered by an influx of Na+ during phase 0 of the action potential. Cardiac muscle cells are so tightly bound that when one of these cells is excited the action potential spreads to all of them. The standard model used to understand the cardiac action potential is the action potential of the ventricular myocyte (Park & Fishman 2011, Grant 2009).

The action potential has 5 phases (numbered 0-4). Phase 4 describes the membrane potential when a cell is not being stimulated. The normal resting potential in the ventricular myocardium is between -85 to -95 mV. The K+ gradient across the cell membrane is the key determinant in the normal resting potential. Phase 0 is the rapid depolarisation phase in which electrical stimulation of a cell opens the closed, fast Na+ channels, causing a large influx of Na+ creating a Na+ current (I_{Na+}). This causes depolarisation of the cell. The slope of phase 0 represents the maximum rate of potential change and differs in contractile and pacemaker cells. Phase 1 is the inactivation of the fast Na+ channels. The transient net outward current causing the small downward deflection (the "notch" of the action potential) is due to the movement of K+ and Cl- ions. In pacemaker cells, this phase is due to rapid K+ efflux and closure of L-type Ca2+ channels. Phase 2 is the plateau phase which is sustained by a balance of Ca2+ influx and K+ efflux. This phase sustains muscle contraction. Phase 3 of the action potential is where a concerted action of two outward delayed currents brings about repolarisation back down to the resting potential (Bartos et al. 2015).

Literature references


### Editions

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Phase 4 describes the membrane potential when a cell is not being stimulated. The normal resting potential in the ventricular myocardium is between -85 to -95 mV. The membrane is most permeable to K+ and relatively impermeable to other ions therefore the K+ gradient across the cell membrane is the key determinant in the normal resting potential (Park & Fishman 2011, Grant 2009). In this phase, K+ currents are generated by inward rectifier potassium channels (KCNJs) and tandem pore domain K+ channels (KCNKs). Some Na+/K+-ATPases and Na+/Ca2+-exchangers can also play roles during this phase.

**Literature references**


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Phase 0 - rapid depolarisation

**Location:** Cardiac conduction

**Stable identifier:** R-HSA-5576892

Phase 0 is the rapid depolarisation phase in which electrical stimulation of a cell initiates events involving the influx and efflux of ions resulting in the production of a cell's action potential. The cell's excitation opens the closed, fast Na+ channel proteins, causing a large influx of Na+ creating a Na+ current \( (I_{Na}) \). This causes depolarisation of the cell then voltage-dependent L-type calcium channels (LTCCs) transport Ca2+ into excitable cells. The slope of phase 0 represents the maximum rate of potential change and differs in contractile and pacemaker cells. The potential in this phase changes from around -90mV to around +50mV (Park & Fishman 2011, Grant 2009).

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Phase 1 - inactivation of fast Na+ channels

Location: Cardiac conduction

Stable identifier: R-HSA-5576894

Phase 1 of the cardiac action potential is the inactivation of the fast Na+ channels. The transient net outward current causing the small downward deflection (the "notch" of the action potential) is due to the movement of K+ and Cl- ions. In pacemaker cells, this phase is due to rapid K+ efflux and closure of L-type Ca2+ channels (Park & Fishman 2011, Grant 2009).

Literature references


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Phase 2 - plateau phase

Location: Cardiac conduction

Stable identifier: R-HSA-5576893

Phase 2 of the cardiac action potential is the plateau phase which is sustained by a balance of Ca2+ influx through L-type Ca2+ channels (LTCCs) and K+ efflux through the slow delayed rectifier K+ channel 1 (KCNQ1). This phase sustains muscle contraction (Park & Fishman 2011, Grant 2009).

Literature references


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Phase 3 - rapid repolarisation

Location: Cardiac conduction

Stable identifier: R-HSA-5576890

In phase 3 (the "rapid repolarisation" phase), the L-type Ca2+ channels close, while the slow delayed rectifier (I_{Ks}) K+ channels remain open as more K+ leak channels open. This ensures a net outward positive current, corresponding to negative change in membrane potential, thus allowing more types of K+ channels to open. These are primarily the rapid delayed rectifier K+ channels (I_{Kr}) and the inwardly rectifying K+ current, I_{K1} (Kir). This net outward, positive current (equal to loss of positive charge from the cell) causes the cell to repolarize. The primary delayed rectifier K+ currents (I_{Ks} and I_{Kr}) are generated by K+ efflux mediated by potassium voltage-gated channel subfamily KQT member 1 (KCNQ1 aka Kv7.1) and potassium voltage-gated channel subfamily H member 2 (KCNH2 aka HERG) channels respectively (Park & Fishman 2011, Grant 2009). Specific to the atria, an ultra-rapidly activating delayed rectifier outward K+ current (I_{Kur}) generated primarily by potassium voltage-gated channel subfamily A member 5 (KCNA5) helps to repolarize atrial cells (Wang et al. 1993, Feng et al. 1997).

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https://reactome.org
Ion homeostasis

Location: Cardiac conduction

Stable identifier: R-HSA-5578775

Ion channels and ion homeostasis in relation to cardiac conduction is described in this section (Couette et al. 2006, Bartos et al. 2015).

Literature references


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Physiological factors

Location: Cardiac conduction

Stable identifier: R-HSA-5578768

Cardiovascular homeostasis can be regulated by natriuretic peptides (Pandey 2014).

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Table of Contents

Introduction 1

* Cardiac conduction 2
  - Phase 4 - resting membrane potential 4
  - Phase 0 - rapid depolarisation 5
  - Phase 1 - inactivation of fast Na+ channels 6
  - Phase 2 - plateau phase 7
  - Phase 3 - rapid repolarisation 8
  - Ion homeostasis 9
  - Physiological factors 10

Table of Contents 11