Editorial Board

Point/Counterpoint

The pathophysiological mechanism underlying Brugada syndrome: Depolarization versus repolarization

Pages 543-553
Arthur A.M. Wilde, Pieter G. Postema, José M. Di Diego, Sami Viskin, Hiroshi Morita, Jeffrey M. Fish, Charles Antzelevitch

Editorial

A “rough‖ journey to the sarcoplasmic reticulum—implications of altered calsequestrin trafficking for cardiac arrhythmia

Pages 554-555
Bjorn C. Knollmann

Highlighted Article

Rough endoplasmic reticulum to junctional sarcoplasmic reticulum trafficking of calsequestrin in adult cardiomyocytes

Original Research Article
Pages 556-564
Timothy P. McFarland, Michelle L. Milstein, Steven E. Cala

Research Highlights

► Cardiac rough ER and CSQ biosynthesis localize to perinuclear cisternae in adult cardiomyocytes. ► CSQ polymerization accounts for its concentration in junctional SR puncta. ► CSQ traffic directly from rough ER to junctional SR along an uncharacterized intracellular pathway. ► Longitudinal SR appears to be distal to junctional SR, and ER exit sites may interact with CSQ.

Regular Articles

Optical imaging of mitochondrial function uncovers actively propagating waves of mitochondrial membrane potential collapse across intact heart

Original Research Article
Pages 565-575
Alexander R. Lyon, Paul J. Joudrey, Dongzhu Jin, Robert D. Nass, Miguel A. Aon, Brian O'Rourke, Fadi G. Akar

4-Hydroxy-2-nonenal protects against cardiac ischemia–reperfusion injury via the Nrf2-dependent pathway

Original Research Article
Chronic AMD3100 antagonism of SDF-1α–CXCR4 exacerbates cardiac dysfunction and remodeling after myocardial infarction

Shujing Dai, Fangping Yuan, Jingyao Mu, Chengxin Li, Ning Chen, Shangzhi Guo, Justin Kingery, Sumanth D. Prabhu, Roberto Bolli, Gregg Rokosh

Research Highlights
► SDF-1α–CXCR4 signaling is necessary during the myocardial response to infarction. ► CXCR4 activation affects signaling through AKT and GSK-3β dependent pathways. ► CXCR4 signaling facilitates myocardial survival, by attenuating cell death. ► CXCR4 promotes cardiac progenitor cells to contribute to myocardial infarction. ► CXCR4 promotes favorable remodeling after myocardial infarction.

Identification of right heart-enriched genes in a murine model of chronic outflow tract obstruction

Karsten grosse Kreymborg, Shizuka Uchida, Pascal Gellert, André Schneider, Thomas Boettger, Robert Voswinckel, Astrid Wietelmann, Marten Szibor, Norbert Weissmann, Ardeschir Hossein Ghofrani, Ralph Schermuly, Dietmar Schranz, Werner Seeger, Thomas Braun

Research Highlights
► New mouse model for chronic right ventricular (RV) hypertrophy. ► Functional characterization of RV hypertrophy model by magnetic resonance imaging. ► Transcriptional profiling of RV hypertrophy model. ► Comparison of transcriptional changes in LV and RV hypertrophy by microarray. ► Identification of novel potential (co)-regulators of long-term RV remodeling.

Epicardium-derived cells enhance proliferation, cellular maturation and alignment of cardiomyocytes


Research Highlights
► Direct contact with epicardium-derived cells (EPDCs) increases proliferation and cytoarchitectural maturation of cardiomyocytes ► This is reflected by increased levels of gap junctions (Cx43), adherens junctions (N-cadherin), SERCA2a, and cellular and sarcomeric alignment of the cardiomyocytes ► Deposition of extracellular matrix and recruitment of FAK are likely to be instrumental in the EPDC-dependent cytoarchitectural maturation of cardiomyocytes and associated with an increase in their contractility.
Research Highlights
► We present a ventricular myocyte model with local LCC and RyR regulation by CaMKII. ► RyR phosphorylation augments ECC gain. LCC phosphorylation reduces gain curve slope. ► Phosphorylation of even large fractions of RyRs modestly affects Ca transients. ► Diastolic SR leak is increased more by LCC than RyR phosphorylation during APs. ► Augmented LCC phosphorylation increases APD and induces EADs.

Benfotiamine improves functional recovery of the infarcted heart via activation of pro-survival G6PD/Akt signaling pathway and modulation of neurohormonal response Original Research Article Pages 625-638
Rajesh Katare, Andrea Caporali, Costanza Emanuelli, Paolo Madeddu

Research Highlights
► Role of pentose shunt pathway in modulation of the post-MI recovery is not known. ► Results of the present study demonstrates a novel treatment modality for chronic MI through activation of glucose-6-phosphate dehydrogenase and transketolase, the major enzymes involved in the pentose shunt pathway. ► Importantly, this study enlighten the mechanism behind poor recovery after MI in diabetic patients.

Gender-related differences in ion-channel and transporter subunit expression in non-diseased human hearts Original Research Article Pages 639-646
Nathalie Gaborit, Andras Varro, Sabrina Le Bouter, Viktoria Szuts, Denis Escande, Stanley Nattel, Sophie Demolombe

IL-19 reduces VSMC activation by regulation of mRNA regulatory factor HuR and reduction of mRNA stability Original Research Article Pages 647-654
Anthony A. Cuneo, David Herrick, Michael V. Autieri

EMMPRIN activates multiple transcription factors in cardiomyocytes, and induces interleukin-18 expression via Rac1-dependent PI3K/Akt/IKK/NF-κB and MKK7/JNK/AP-1 signaling Original Research Article Pages 655-663
Balachandar Venkatesan, Anthony J. Valente, Sumanth D. Prabhu, Prakashsrinivasan Shanmugam, Patrice Delafontaine, Bysani Chandrasekar

Research Highlights
► EMMPRIN activates the transcription factors NF-κB, AP-1, CREB and ATF-2 in cardiomyocytes. ► EMMPRIN stimulates IL-18 expression via Rac1-dependent PI3K/NF-κB and MKK7/AP-1 activation. ► EMMPRIN induces time-dependent MMP and TIMP expression.

NF-κB driven cardioprotective gene programs; Hsp70.3 and cardioprotection after late ischemic preconditioning Original Research Article Pages 664-672
Michael Tranter, Xiaoping Ren, Tiffany Forde, Michael E. Wilhide, Jing Chen,
Maureen A. Sartor, Mario Medvedovic, W. Keith Jones

Research highlights

► Our results show that NF-κB regulates a unique set of 238 genes after late IPC; several of these have been previously implicated in late IPC. ► NF-κB regulates genes that fall primarily into three functional categories; angiogenesis, programmed cell death and heat shock response. ► One of these genes, Hsp70.3, is shown to be functionally cardioprotective, while the related Hsp70.1 is not. ► Hsp 70.1 is injurious after I/R injury, and thus functionally opposed to Hsp70.3. ► NF-κB thus regulates multiple genes which contribute to late IPC.

Lmcd1/Dyxin, a novel Z-disc associated LIM protein, mediates cardiac hypertrophy in vitro and in vivo Original Research Article
Pages 673-682
Derk Frank, Robert Frauen, Christiane Hanselmann, Christian Kuhn, Rainer Will, Johanne Gantenberg, Laszlo Füzesi, Hugo A. Katus, Norbert Frey

Research highlights

► The novel sarcomeric Z-disc LIM protein Lmcd1/Dyxin is upregulated by stretch and phenylephrine in cardiomyocytes (NRCM) ► Dyxin/Lmcd1 is induced in several mouse models of myocardial hypertrophy ► Overexpressed Dyxin/Lmcd1 leads to hypertrophy in NRCM ► Knockdown of Lmcd1 blunts the response to hypertrophic stimuli by blocking calcineurin activation ► Transgenic overexpression of Dyxin/Lmcd1 causes cardiac hypertrophy in vivo which is accompanied by activation of calcineurin signaling ► Lmcd1/Dyxin may thus represent an attractive target for novel antihypertrophic strategies.

SGLT1, a novel cardiac glucose transporter, mediates increased glucose uptake in PRKAG2 cardiomyopathy Original Research Article
Pages 683-692
Sanjay K. Banerjee, David W. Wang, Rodrigo Alzamora, Xueyin N. Huang, Núria M. Pastor-Soler, Kenneth R. Hallows, Kenneth R. McGaffin, Ferhaan Ahmad

Research Highlights

► SGLT1 is upregulated in transgenic mice with the T400N mutation in PRKAG2 (TG T400N). ► SGLT1 at least partially mediates increased cardiac glucose uptake in TG T400N mice. ► The cardiomyopathy phenotype is partially attenuated by inhibition of SGLT1. ► Upregulation of cardiac SGLT1 is caused by AMPK activity.

Transient upregulation of PGC-1α diminishes cardiac ischemia tolerance via upregulation of ANT1 Original Research Article
Pages 693-698
Edward G. Lynn, Mark V. Stevens, Renee P. Wong, Darin Carabenciov, Jeremy Jacobson, Elizabeth Murphy, Michael N. Sack

Right ventricular remodeling in restrictive ventricular septal defect Original Research Article
Pages 699-706
Gretel Monreal, Dane J. Youtz, Alistair B. Phillips, Mahala E. Eyman, Matthew W. Gorr,
Research highlights

► Restrictive ventricular septal defect (rVSD) results in remodeling of the RV. ► rVSD causes RV diastolic dysfunction and impaired myocyte contraction/relaxation. ► Desmin is upregulated in rVSD and is a subclinical biomarker for RV remodeling. ► Patients with rVSD should be carefully examined for RV diastolic dysfunction. ► These findings may improve patient care by providing data for early repair of rVSD.

Letters to the Editor

Frank–Starling law and mass action calcium activation of the myofibril ATPase; Comment on “de Tombe PP, Mateja RD, Tachampa K, Mou YA, Farman GP, Irving TC. Myofilament length dependent activation. J Mol Cell Cardiol 2010; 48: 851–8”
Pages 707-708
Gerry A. Smith

Reply to Smith letter: Controversy persists after over 100 years of the Frank–Starling mechanism
Page 709
R. John Solaro, Pieter P. de Tombe