How does the shape of the cardiac action potential control calcium signaling and contraction in the heart?

Luis F. Santana, Edward P. Cheng, W. Jonathan Lederer

The therapeutic potential of heat shock proteins in cardiomyopathies due to mutations in cardiac structural proteins

Jessica E. Rodríguez, Monte S. Willis

Rab4a signaling unmasks a pivotal link between myocardial homeostasis and metabolic remodeling in the diabetic heart

Michael N. Sack

Excitation–contraction coupling in human heart failure examined by action potential clamp in rat cardiac myocytes

Patricia J. Cooper, Christian Soeller, Mark B. Cannell

Selective degradation of aggregate-prone CryAB mutants by HSPB1 is mediated by ubiquitin–proteasome pathways

Huali Zhang, Namakkal S. Rajasekaran, Andras Orosz, Xianzhong Xiao, Martin Rechsteiner, Ivor J. Benjamin

Akt2 deficiency promotes cardiac induction of Rab4a and myocardial β-adrenergic hypersensitivity

Sharon Etzion, Yoram Etzion, Brian DeBosch, Peter A. Crawford, Anthony J. Muslin

Research highlights

- HSPB1 overexpression has differential effects on the solubility of aggregate-prone CryAB mutants. HSPB1 knockdown decreased solubility and increased aggregates of all CryAB mutants. Selective clearance of CryAB mutants by HSPB1 is mediated by UPS.

Research Highlights
Rab4a promotes β-adrenergic receptor recycling to the plasma membrane. Akt2 deficiency leads to increased myocardial Rab4a. PPARα activation leads to increased myocardial Rab4a. Akt2 deficiency increases myocardial β-adrenergic sensitivity. Akt2 deficiency and PPARα activation lead to propranolol-responsive cardiac hypertrophy.

**Regular Articles**

**Human embryonic stem cell-derived cardiomyocytes engraft but do not alter cardiac remodeling after chronic infarction in rats**

Original Research Article

Pages 941-949

S. Fernandes, A.V. Naumova, W.Z. Zhu, M.A. Laflamme, J. Gold, C.E. Murry

**Research Highlights**

► hESC-CM can engraft when injected in a chronic model of myocardial infarction. ► hESC-CM survived at least as well as was previously observed in an acute infarction model. ► hESC-CM transplantation does not alter adverse remodeling of a chronic infarction model.

**Mitochondrial complex II participates in normoxic and hypoxic regulation of α-keto acids in the murine heart**

Original Research Article

Pages 950-961

Jörg Mühling, Martina Tiefenbach, José López-Barneo, José I. Piruat, Paula García-Flores, Uwe Pfeil, Barbara Gries, Christian Mühlfeld, Markus A. Weigand, Wolfgang Kummer, Norbert Weissmann, Renate Paddenberg

**Research Highlights**

► Right ventricular hypertrophy is less severe in SDHD+/− mice as compared to WT. ► Protein amounts of SDHA, SDHB and SDHC, and SDH activity are distinctly reduced in SDHD+/− mice. ► In normoxic SDHD+/− mice, α-ketoisocaprate concentration is lowered to 50% as compared to WT animals. ► Right/left ventricular differences and the hypoxic decline in individual α-KAs are less pronounced in SDHD+/− animals. ► Mitochondrial morphometric parameters are comparable in WT and SDHD+/− mice housed at normoxia or hypoxia.

**Stretch increases the force by decreasing cross-bridge weakening rate in the rat cardiac trabeculae**

Original Research Article

Pages 962-971

Moran Yadid, Amir Landesberg

**Research Highlights**

► Stretch increases the force by decreasing the cross-bridge cycling rate. ► The stress and stiffness development rates are linear functions of the velocity. ► The force per cross-bridge is constant and identical at all stretch velocities. ► The force and stiffness increase in parallel during isovelocity stretches. ► These phenomena are independent of the stretch onset time (activation level).

**Implantation of cardiac progenitor cells using self-assembling peptide improves cardiac function after myocardial infarction**

Original Research Article

Pages 972-983

Masakuni Tokunaga, Mei-Lan Liu, Toshio Nagai, Koji Iwanaga, Katsuhisa Matsuura, Toshinao Takahashi, Masato Kanda, Naomichi Kondo, Pin Wang, Atsuhide T. Naito, Issei Komuro
Research Highlights

►Implantation of cardiac progenitor cells reduces infarct size in comparison with other cell types. ►Implantation of cardiac progenitor cells promotes angiogenesis, survival of cardiomyocytes. ►Implanted cardiac progenitor cells differentiate into cardiomyocytes and smooth muscle cells. ►Self-assembling peptide is useful to facilitate the engraftment of cardiac progenitor cells.

**Celecoxib blocks cardiac Kv1.5, Kv4.3 and Kv7.1 (KCNQ1) channels: Effects on cardiac action potentials** Original Research Article
Pages 984-992
Álvaro Macías, Cristina Moreno, Javier Moral-Sanz, Ángel Cogolludo, Miren David, Matteo Alemanni, Francisco Pérez-Vizcaíno, Antonio Zaza, Carmen Valenzuela, Teresa González

Research Highlights

►Celecoxib blocks Kv1.5 channels (I_{Kur}) independently of COX-2 inhibition. ►Celecoxib blocks Kv4.3 + KChIP2 (I_{to}) and Kv7.1 + KCNE1 (I_{Ks}) channels. ►Celecoxib might influence myocardial repolarization via its inhibitory effects on Kv channels.

**Neonatal gene transfer of Serca2a delays onset of hypertrophic remodeling and improves function in familial hypertrophic cardiomyopathy** Original Research Article
Pages 993-1002

Research Highlights

►Serca2a should be considered as a potential target for gene therapy not only in patients with late stages of HF, but also in patients with FHC. ►Therapies for FHC may be more successful if started shortly after birth.

**Analysis of cardiac myosin binding protein-C phosphorylation in human heart muscle** Original Research Article
Pages 1003-1011
O'Neal Copeland, Sakthivel Sadayappan, Andrew E. Messer, Ger J.M. Steinern, Jolanda van der Velden, Steven B. Marston

**Graphical abstract**
Research Highlights

► At least 4 sites are phosphorylated at in human heart muscle MyBP-C. ► In donor heart 4P and 3P species predominate and the total phosphorylation level is 2.7 molPi/mol. ► In failing heart and in myectomy samples the phosphorylation is greatly reduced. ► Site-specific antibodies show that 273P, 286P and 302P are present in the 4P band but none of these are in the 1P band.

EBP50 inhibits the anti-mitogenic action of the parathyroid hormone type 1 receptor in vascular smooth muscle cells

Gyun Jee Song, Stacey Barrick, Kristen L. Leslie, Brian Sicari, Nathalie M. Fiaschi-Taesch, Alessandro Bisello

Research Highlights

► EBP50 expression increases in the neointima following angioplasty. ► EBP50 regulates PTH1R expression and G protein signaling. ► EBP50 is necessary for PTH1R-mediated increase in p27kip1. ► EBP50 abrogates PTHrP(1–36)-dependent inhibition of VSMC proliferation.

Effects of neuropeptide Y on collateral development in a swine model of chronic myocardial ischemia

Michael P. Robich, Robina Matyal, Louis M. Chu, Jun Feng, Shu-Hua Xu, Roger J. Laham, Philip E. Hess, Cesario Bianchi, Frank W. Sellke

Research Highlights

► Neuropeptide Y (NPY) is a 36 kDa mediator of neurogenic angiogenesis. ► Exogenous NPY in ischemic swine improved myocardial function, collateral formation. ► NPY stimulated pro-angiogenic receptor upregulation. ► NPY decreased anti-angiogenic protein expression. ► NPY may act as a good adjunct to primary agents of therapeutic angiogenesis.

A structural and functional perspective into the mechanism of Ca²⁺-sensitizers that target the cardiac troponin complex

Ian M. Robertson, Yin-Biao Sun, Monica X. Li, Brian D. Sykes

Research Highlights
**Rapid Communication**

Migration and proliferation of human mesenchymal stem cells is stimulated by different regions of the mechano-growth factor prohormone

*Pages 1042-1045*

John M. Collins, Paul H. Goldspink, Brenda Russell

**Research Highlights**

- Migration of human mesenchymal stem cells increased with MGF-E peptide.
- A serine to alanine substitution in MGF-E reduced migration significantly.
- IGF-1 polypeptide increased proliferation of small but not large cells.
- MGF-E had no effect on human mesenchymal stem cell proliferation.
- Cyclic strain induces MGF-E in neonatal myocytes but not mesenchymal stem cells.