

Circulation Research

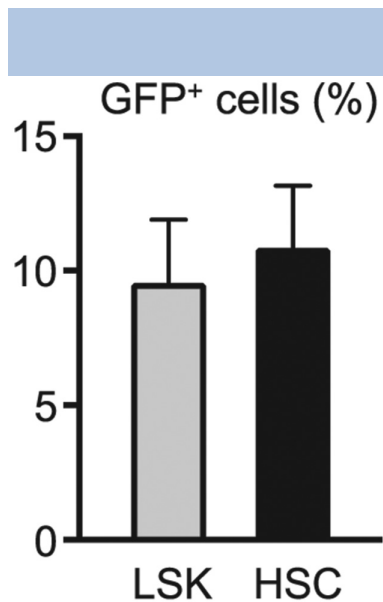
Volume 123 Number 3 July 20, 2018

★ **Featured Article**

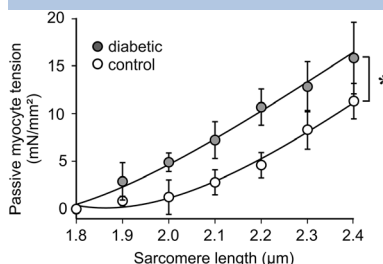
📎 Online supplementary information

🎬 Online movie files

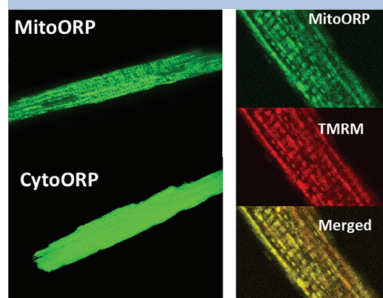
Available at <http://circres.ahajournals.org>



Hematopoietic Tet2, Dnmt3a, and Heart Failure
Sano *et al.* page 335



Titin-Based Stiffness in Diabetic Hearts
Hopf *et al.* page 342



mROS Drive Sudden Death and Heart Failure
Dey *et al.* page 356

In This Issue 309

Meet the First Authors 310

Editorials

A CRISPR Take on Clonal Hematopoiesis
Filip K. Swirski 313

Softening the Stressed Giant Titin in Diabetes Mellitus
Mei Methawasin, Henk Granzier 315

Trainees in the Spotlight

David M. Ryba: Pushing the Field Forward
Pam Goldberg-Smith 318

Leaders in Cardiovascular Science

José Jalife: Perseverance Pays Off
Ruth Williams 320

News & Views

Leducq Network: Modulating Autophagy to Treat Cardiovascular Disease
Julio Madrigal-Matute, Luca Scorrano, Junichi Sadoshima 323

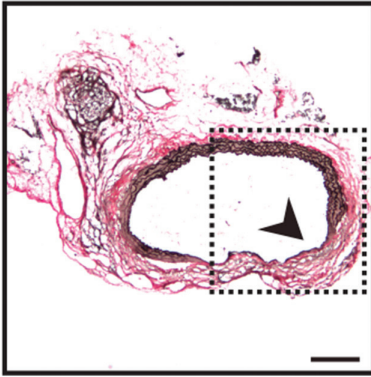
Viewpoints

Redox Regulation Beyond ROS: Why ROS Should Not Be Measured as Often
Ralf P. Brandes, Flavia Rezende, Katrin Schröder **OPEN** 326

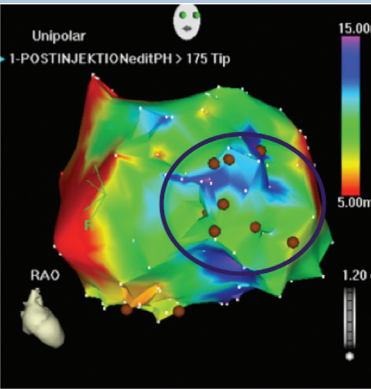
Effective Metabolic Approaches for the Energy Starved Failing Heart: Bioenergetic Resiliency via Redundancy or Something Else?
Jianyi Zhang, E. Dale Abel 329

Mouse Models of Cardiac Arrhythmias
Dobromir Dobrev, Xander H.T. Wehrens 332

CIRCULATION RESEARCH (ISSN 0009-7330 print / 1524-4571 online) is published semimonthly for 24 total issues a year by Wolters Kluwer Health, Inc. at 14700 Citicorp Drive, Bldg 3, Hagerstown, MD 21742. Business offices are located at Two Commerce Square, 2001 Market Street, Philadelphia, PA 19103. Production offices are located at 351 West Camden Street, Baltimore, MD 21201-2436. Individuals may subscribe for their personal use at the following rates for print subscriptions: \$225 for AHA/ASA Domestic and International Members (excluding General Membership level), or \$833 for domestic non-members and \$989 for international non-members. AHA membership information can be found online at professional.heart.org. Periodicals postage paid at Hagerstown, MD, and additional mailing offices. POSTMASTER: Send address changes to *Circulation Research*, American Heart Association, Wolters Kluwer Health, Inc., PO Box 1610, Hagerstown, MD 21740.



Vascular ADAM17 in Thoracic Aortic Aneurysm
Shen *et al.* page 372



Repetitive CD34⁺ Cell Therapy in Cardiomyopathy
Vrtovec *et al.* page 389

Brief UltraRapid Communication

★ CRISPR-Mediated Gene Editing to Assess the Roles of Tet2 and Dnmt3a in Clonal Hematopoiesis and Cardiovascular Disease

Soichi Sano, Kosei Oshima, Ying Wang, Yasufumi Katanasaka, Miho Sano, Kenneth Walsh

335

Molecular Medicine

★ Diabetes-Induced Cardiomyocyte Passive Stiffening Is Caused by Impaired Insulin-Dependent Titin Modification and Can Be Modulated by Neuregulin-1

Anna-Eliane Hopf, Christian Andresen, Sebastian Kötter, Małgorzata Isić, Kamila Ulrich, Senem Sahin, Sabine Bongardt, Wilhelm Röhl, Felicitas Drove, Nina Scheerer, Leni Vandekerckhove, Gilles W. De Keulenaer, Nazha Hamdani, Wolfgang A. Linke, Martina Krüger

342

★ Mitochondrial ROS Drive Sudden Cardiac Death and Chronic Proteome Remodeling in Heart Failure

Swati Dey, Deeptankar DeMazumder, Agnieszka Sidor, D. Brian Foster, Brian O'Rourke

356

Integrative Physiology

Cell-Specific Functions of ADAM17 Regulate the Progression of Thoracic Aortic Aneurysm

Mengcheng Shen, Mei Hu, Paul W.M. Fedak, Gavin Y. Oudit, Zamaneh Kassiri 372

Clinical Track

★ Effects of Repetitive Transendocardial CD34⁺ Cell Transplantation in Patients With Nonischemic Dilated Cardiomyopathy

Bojan Vrtovec, Gregor Poglajen, Matjaz Sever, Gregor Zemljic, Sabina Frljak, Andraz Cerar, Marko Cukjati, Martina Jaklic, Peter Cernelc, François Haddad, Joseph C. Wu

389

In May 2018, the average time from submission to first decision for all original research papers submitted to *Circulation Research* was 13.28 days.

On the Cover: CRISPR/Cas9 gene editing was applied to the study of clonal hematopoiesis and cardiovascular disease. Hematopoietic stem cells were infected with lentivirus expressing CRISPR/Cas9 and gRNA targeting Tet2 or Dnmt3a. Gene-edited cells were transplanted into irradiated mice. Mice harboring mutant hematopoietic cells showed greater deterioration in a heart failure model. Cover illustration by Ben Smith. See related article, page 335.