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Muscle expression of a malonyl-CoA-insensitive carnitine palmitoyltransferase-1 protects mice against high-fat/high-sucrose diet-induced insulin resistance
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Some problems with translating the insulating effect of obesity from mice to men
Ollie Jay, David Raubenheimer
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Reply to letter to the editor: at thermoneutrality, neither the lean nor the obese freeze
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DOI: 10.1152/ajpendo.00309.2016

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How host regulation of Helicobacter pylori-induced gastritis protects against peptic ulcer disease and gastric cancer
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Editorial Focus

Long noncoding RNAs: novel links to inflammatory bowel disease?
Laura E. Edgington-Mitchell
September 1, 2016 : G444-G445
DOI: 10.1152/ajpgi.00271.2016

Translational Physiology

Effect of nitrate supplementation on hepatic blood flow and glucose homeostasis: a double-blind, placebo-controlled, randomized control trial
Anthony I. Shepherd, Daryl P. Wilkerson, Jon Fulford, Paul G. Winyard, Nigel Benjamin, Angela C. Shore, Mark Gilchrist
September 1, 2016 : G356-G364
DOI: 10.1152/ajpgi.00203.2016

This is the first study investigating the effect dietary nitrate supplementation on hepatic blood flow and on incretin and C-peptide concentrations in young and older adults. Despite a physiologically relevant elevation in plasma nitrite concentration following an acute dose of 11.9 nmol nitrate, there was no effect on hepatic blood flow, plasma glucose, C-peptide, or incretin concentration. Acute supplementation of nitrate does not appear to alter hepatic diffusion or modulate postprandial glucose homeostasis.

Preterm infant gut microbiota affects intestinal epithelial development in a humanized microbiome gnotobiotic mouse model
Yueyue Yu, Lei Lu, Jun Sun, Elaine O. Petrof, Erika C. Claud
September 1, 2016 : G521-G532
DOI: 10.1152/ajpgi.00022.2016

Changes in the microbiome early in life may affect host physiology across the life span. Early life interaction between host and luminal microbes was investigated using a mouse model in which germ-free mice were transfaunated with fecal lysates from human preterm infants. Our data
demonstrate that microbial communities affect differentiation of intestinal epithelial cell lineages, which may lead to significant effects on developmental, defensive, and physiological processes of the gastrointestinal epithelium.

Epithelial Biology and Secretion

Redox control of Cas phosphorylation requires Abl kinase in regulation of intestinal epithelial cell spreading and migration
Jason D. Matthews, Ronen Sumagin, Benjamin Hinrichs, Asma Nusrat, Charles A. Parkos, Andrew S. Neish
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Neurogastroenterology and Motility

Pilot study of small bowel mucosal gene expression in patients with irritable bowel syndrome with diarrhea
Michael Camilleri, Paula Carlson, Nelson Valentin, Andres Acosta, Jessica O'Neill, Deborah Eckert, Roy Dyer, Jie Na, Eric W. Klee, Joseph A. Murray
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DOI: 10.1152/ajpgi.00037.2016

Liver and Biliary Tract Physiology/Pathophysiology

Autophagy confers resistance to lipopolysaccharide-induced mouse hepatocyte injury
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September 1, 2016 : G377-G386
DOI: 10.1152/ajpgi.00124.2016

A return to ad libitum feeding following caloric restriction promotes hepatic steatosis in hyperphagic OLETF rats
Melissa A. Linden, Justin A. Fletcher, Grace M. Meers, John P. Thyfault, M. Harold Laughlin, R. Scott Rector
September 1, 2016 : G387-G395
DOI: 10.1152/ajpgi.00089.2016

Caloric restriction-induced prevention of nonalcoholic fatty liver disease (NAFLD) is lost after only 4 wk of ad libitum feeding in hyperphagic Otsuka Long-Evans Tokushima fatty rats despite only modest increases in body weight and adiposity. While some beneficial hepatic mitochondrial adaptations were maintained, NAFLD development occurred in conjunction with dramatic increases in hepatic de novo lipogenesis. These findings suggest that prior caloric restriction offers little metabolic protection against future development of NAFLD should healthy eating patterns not persist.

Neurogastroenterology and Motility

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Macrophage colony-stimulating factor (CSF1) controls monocyte production and maturation and the steady-state size of the liver in pigs

Kristin A. Sauter, Lindsey A. Waddell, Zofia M. Lisowski, Rachel Young, Lucas Lefevre, Gemma M. Davis, Sara M. Clohisey, Mary McCulloch, Elizabeth Magowan, Neil A. Mabbott, Kim M. Summers, David A. Hume
September 1, 2016 : G533-G547

DOI: 10.1152/ajpgi.00027.2016

This study is based on extensive studies in the mouse of the role of CSF1 in monocyte-macrophage production and differentiation and the function of macrophages in the control of hepatocyte proliferation. We use a novel form of CSF1, an Fc fusion protein, to demonstrate that the findings in mice can be extended to large animals. We discuss the possible role for CSF1 in homeostatic control of the size of the liver.

Pancreatic Physiology/Pathophysiology

PanIN-associated pericyte, glial, and islet remodeling in mice revealed by 3D pancreatic duct lesion histology

Pei-Yu Lin, Shih-Jung Peng, Chia-Ning Shen, Pankaj J. Pasricha, Shiue-Cheng Tang
September 1, 2016 : G412-G422

DOI: 10.1152/ajpgi.00071.2016

Transparent mouse pancreata with an acinar KrasG12D mutation were prepared by optical clearing to develop 3D duct lesion histology. This imaging approach identifies perilesional pericyte and glial activation and formation of pancreatic intraepithelial neoplasia (PanIN)-islet complexes, which otherwise cannot be easily portrayed by standard 2D tissue analysis. Our results highlight the cellular heterogeneity in the PanIN microenvironment and reveal anatomic details of neurovascular and endocrine links to the disease.

Legumain is activated in macrophages during pancreatitis

September 1, 2016 : G548-G560

DOI: 10.1152/ajpgi.00047.2016

Proteases are important mediators of many inflammatory diseases, including pancreatitis. With the use of recently developed chemical tools, activity of the cysteine protease legumain was found to be upregulated in acute and chronic pancreatitis. While legumain activity appears to be dispensable for initiation of pancreatitis, it serves as a biomarker for infiltrating macrophages in both mouse and human disease. Since legumain is enriched in areas of acinar-to-ductal metaplasia, it may function to promote the transition from chronic inflammation to cancer.

Inflammation, Immunity, Fibrosis, and Infection

A long noncoding RNA signature for ulcerative colitis identifies IFNG-AS1 as an enhancer of inflammation

David Padua, Swapna Mahurkar-Joshi, Ivy Ka Man Law, Christos Polytauchour, John P. Vu, Joseph R. Pisegna, David Shih, Dimitrios Iliopoulos, Charalabos Pothoulakis
September 1, 2016 : G446-G457

DOI: 10.1152/ajpgi.00212.2016

Long noncoding RNA (lncRNA) biology represents an exciting new field with implications in gene regulation. This field has only recently been investigated in the pathogenesis of ulcerative colitis. By utilizing high-throughput technologies on clinical samples, a lncRNA signature was generated and the lncRNA IFNG-AS1 was shown to regulate the important inflammatory cytokine interferon-γ. This work represents one of the first mechanistic studies of lncRNA biology in inflammatory bowel disease.

Microbiome and Host Interactions

Identification of food-grade subtilisins as gluten-degrading enzymes to treat celiac disease

Guoxian Wei, Na Tian, Roland Siezen, Detlef Schuppan, Eva J. Helmerhorst
September 1, 2016 : G571-G580

DOI: 10.1152/ajpgi.00185.2016

A novel class of gluten-degrading enzymes were isolated from Rothia bacteria, which are natural colonizers of the oral cavity. The enzymes were identified as subtilisins belonging to the S8 family of peptidases. Food-grade Bacillus species also produce such subtilisins, and these were also able to cleave and abolish gluten immunogenic epitopes. Subtilisins, cleaving after XPX↓, represent an as yet overlooked class of enzymes with great
potential for enzyme therapeutic applications in celiac disease.

**Nutrient Sensing, Nutrition, and Metabolism**

**Intestinal brush-border Na\(^+\)/H\(^+\) exchanger-3 drives H\(^+\)-coupled iron absorption in the mouse**

September 1, 2016 : G423-G430

DOI: 10.1152/ajpgi.00167.2016

Iron homeostasis is of significant public health interest because of the prevalence of iron deficiency and iron-overload disorders. Whole body iron homeostasis is achieved by regulating iron absorption. We have identified a role for the intestinal brush-border Na\(^+\)/H\(^+\) exchanger-3 in generating the proton-motive force driving iron uptake via the proton-coupled divalent metal-ion transporter-1 and, thereby, energizing intestinal iron absorption.

**Bovine colostrum improves neonatal growth, digestive function, and gut immunity relative to donor human milk and infant formula in preterm pigs**
Stine O. Rasmussen, Lena Martin, Mette V. Østergaard, Silvia Rudloff, Yanqi Li, Michael Roggenbuck, Stine B. Bering, Per T. Sangild

September 1, 2016 : G480-G491

DOI: 10.1152/ajpgi.00139.2016

Even slow advancement of preterm infant formula leads to gut complications in preterm pigs, relative to bovine colostrum. Pasteurized human donor milk fails to support gut protection beyond the first week after preterm birth, at least in pigs. The immature gut shows highly diet-dependent responses to the first enteral feeding, suggesting that diet-dependent feeding guidelines may be required for preterm infants.

**Malabsorption and intestinal adaptation after one anastomosis gastric bypass compared with Roux-en-Y gastric bypass in rats**
Jean-Baptiste Cavin, Eglantine Voitellier, Françoise Cluzeaud, Nathalie Kapel, Jean-Pierre Marmuse, Jean-Marc Chevallier, Simon Msika, André Bado, Maude Le Gall

September 1, 2016 : G492-G500

DOI: 10.1152/ajpgi.00197.2016

Considered simpler and safer than the Roux-en-Y gastric bypass (RYGB), the mini-gastric bypass (MGB) is increasingly performed worldwide. Here we present the first rat model of MGB whose outcomes were compared with those of RYGB. MGB led to similar improvement of glucose tolerance but increased fecal nitrogen and energy loss in rats. These results suggest protein malabsorption after MGB despite intestinal overgrowth and higher expression of peptide transporters. Our study urges direct investigations in humans.

**Role of the sodium-dependent multivitamin transporter (SMVT) in the maintenance of intestinal mucosal integrity**

September 1, 2016 : G561-G570

DOI: 10.1152/ajpgi.00240.2016

This study presents new findings on the role of the intestinal biotin transporter (sodium-dependent multivitamin transporter) in the maintenance of normal intestinal mucosal integrity and health. This effect appears to be mediated, at least in part, via providing cells of the gut mucosa (like immune cells) with the essential micronutrient biotin, whose role in immune function has been reported with increased frequency in recent years.

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In with the new and out with the old: enter multivariate wavelet decomposition, exit transfer function
Aaron A. Phillips, Alex Hansen, Andrei V. Krassioukov
September 7, 2016 : H735-H737
DOI: 10.1152/ajpheart.00512.2016

CALL FOR PAPERS | Cardiovascular Mitochondria and Redox Control in Health and Disease
Twinkle overexpression prevents cardiac rupture after myocardial infarction by alleviating impaired mitochondrial biogenesis
Takahiro Inoue, Masataka Ikeda, Tomomi Ide, Takeo Fujino, Yuka Matsuo, Shinobu Arai, Keita Saku, Kenji Sunagawa
September 1, 2016 : H509-H519
DOI: 10.1152/ajpheart.00044.2016

The roles of mtDNA and mitochondria in the failing myocardium are well studied, but those in cardiac rupture remain unknown. Here, we demonstrated that impaired mitochondrial biogenesis accompanied by increased apoptosis and oxidative stress underlies cardiac rupture, and that mtDNA and mitochondria are potential therapeutic targets for cardiac rupture.

CALL FOR PAPERS | Quantitative Analyses of Coronary Vascular and Cardiac Mechanics in Health and Disease
Left ventricular twist mechanics in the context of normal physiology and cardiovascular disease: a review of studies using speckle tracking echocardiography
Eric J. Stöhr, Rob E. Shave, Aaron L. Baggish, Rory B. Weiner
September 1, 2016 : H633-H644
DOI: 10.1152/ajpheart.00104.2016

The influence of elective percutaneous coronary intervention on microvascular resistance: a serial assessment using the index of microcirculatory resistance
Tadashi Murai, Tetsumin Lee, Yoshihisa Kanaji, Junji Matsuda, Eisuke Usui, Makoto Araki, Takayuki Niida, Keiichi Hishikari, Sadamitsu Ichijyo, Rikuta Hamaya, Taishi Yonetsu, Mitsuaki Isobe, Tsunekazu Kakuta
September 1, 2016 : H520-H531
DOI: 10.1152/ajpheart.00837.2015

Change in microvascular resistance (MR) after percutaneous coronary intervention (PCI) showed a wide range of distribution depending on pre-PCI MR. Until follow-up, overall hyperemic MR significantly decreased with coronary flow increase. The modified hyperemic MR introduced by PCI may affect post-PCI coronary flow.

Functional assessment of the stenotic carotid artery by CFD-based pressure gradient evaluation
Xin Liu, Heye Zhang, Lijie Ren, Huahua Xiong, Zhifan Gao, Pengcheng Xu, Wenhua Huang, Wanqing Wu
September 1, 2016 : H645-H653
DOI: 10.1152/ajpheart.00088.2015

This hemodynamic parameter evaluation shows great potential for improving the accuracy of the classification of the severity of carotid stenosis.

CALL FOR PAPERS | Small Vessels-Big Problems: Novel Insights into Microvascular Mechanisms of Diseases
Pericapillary basement membrane thickening in human skeletal muscles
Oliver Baum, Marius Bigler
September 1, 2016 : H654-H666
DOI: 10.1152/ajpheart.00048.2016

Neurovascular cross talk in diabetic retinopathy: Pathophysiological roles and therapeutic implications
Elizabeth P. Moran, Zhongxiao Wang, Jing Chen, Przemyslaw Sapieha, Lois E. H. Smith, Jian-xing Ma
September 7, 2016 : H738-H749
DOI: 10.1152/ajpheart.00005.2016

Cardiac Excitation and Contraction
CaMKII-dependent phosphorylation regulates basal cardiac pacemaker function via modulation of local Ca\textsuperscript{2+} releases
Elevated basal level of activated CaMKII in intact rabbit sinoatrial node cells leads to high basal CaMKII-dependent protein phosphorylation that is critically important for generation of spontaneous local subsarcolemmal Ca$^{2+}$ releases and normal pacemaker cell automaticity. CaMKII inhibition prevents generation of local Ca$^{2+}$ releases and suppresses spontaneous beating of sinoatrial node cells.

Ventricular stimulus site influences dynamic dispersion of repolarization in the intact human heart

Spatial variation of restitution in relation to varying stimulus site is poorly defined in the intact human heart. Repolarization gradients were shown to be dependent on site of activation with epicardial stimulation promoting significant transmural gradients. Steep restitution slopes were predominant in the normal ventricle.

Partial $I_{K1}$ blockade destabilizes spiral wave rotation center without inducing wave breakup and facilitates termination of reentrant arrhythmias in ventricles

High-resolution optical mapping of two-dimensional rabbit ventricular myocardium has revealed that partial inward rectifier $K^+$ current blockade by Ba$^{2+}$ destabilizes the rotation center of spiral wave re-entry without inducing wave breakup through mechanisms involving an enhancement of electrotonic interactions, prolongation of wavelength, and reduction of excitability and facilitates termination of ventricular tachyarrhythmia.

Cardiovascular Neurohormonal Regulation

Endogenous nitric oxide derived from NOS I or II in thoracic spinal cord exerts opposing tonic modulation on sympathetic vasomotor tone via disparate mechanisms in anesthetized rats

Myocardial energetics is not compromised during compensated hypertrophy in the Dahl salt-sensitive rat model of hypertension

Energetics and Metabolism

A high-salt diet promotes systemic hypertension, which leads the heart to undergo hypertrophy that may progress to failure. We have performed a systematic study on a salt-sensitive rat model of hypertension, which rules out mechanoenergetic changes that were previously implicated in the progression to heart failure.

Right ventricular metabolic adaptations to high-intensity interval and moderate-intensity continuous training in healthy middle-aged men

This is the first study to investigate the effects of exercise training on the right ventricular metabolism of healthy subjects using positron emission tomography. Only 2 wk of either high-intensity interval or moderate-intensity continuous training induces changes in right ventricular glucose metabolism.
metabolism, volumes, and ejection fraction in previously sedentary men.

The von Hippel-Lindau Chuvash mutation in mice alters cardiac substrate and high-energy phosphate metabolism
Mary Slingo, Mark Cole, Carolyn Carr, Mary K. Curtis, Michael Dodd, Lucia Giles, Lisa C. Heather, Damian Tyler, Kieran Clarke, Peter A. Robbins
September 7, 2016: H759-H767
DOI: 10.1152/ajpheart.00912.2015

This is the first integrative metabolic and functional study of the effects of modest hypoxia-inducible factor manipulation within the heart. Of particular note, the combination (and correlation) of perfused heart metabolic flux measurements with the new technique of real-time in vivo magnetic resonance spectroscopy using hyperpolarized pyruvate is a novel development.

Dietary omega-6 fatty acid replacement selectively impairs cardiac functional recovery after ischemia in female (but not male) rats
Wendy T. K. Ip, Andrew McAlindon, Sarah E. Miller, James R. Bell, Claire L. Curl, Catherine E. Huggins, Kimberly M. Mellor, Antonia J. A. Raaijmakers, Laura A. Bienvenu, Peter L. McLennan, Salvatore Pepe, Lea M. D. Delbridge
September 7, 2016: H768-H780
DOI: 10.1152/ajpheart.00690.2015

With the use of stringently controlled diet treatments, this research provides novel evidence at both the heart and cardiomyocyte levels that dietary saturated fatty acid intake replacement with omega-6 (but not omega-3) enriched diet has selective adverse functional effect in females. This finding has potential relevance relating to women, cardiac risk, and dietary management.

Integrative Cardiovascular Physiology and Pathophysiology

Selective serotonin reuptake inhibitor exposure constricts the mouse ductus arteriosus in utero
Christopher W. Hooper, Cassidy Delaney, Taylor Streeter, Michael T. Yarboro, Stanley Poole, Naoko Brown, James C. Slaughter, Robert B. Cotton, Jeff Reese, Elaine L. Shelton
September 1, 2016: H572-H581
DOI: 10.1152/ajpheart.00822.2015

This study is the first to elucidate a mechanism by which serotonin reuptake inhibitors (SSRIs) alter ductus arteriosus tone. It also puts forth the notion that SSRIs may contribute to persistent pulmonary hypertension of the newborn by causing premature fetal ductus constriction.

A gap junction inhibitor, carbenoxolone, induces spatiotemporal dispersion of renal cortical perfusion and impairs autoregulation
Nicholas Mitrou, Branko Braam, William A. Cupples
September 1, 2016: H582-H591
DOI: 10.1152/ajpheart.00941.2015

In vivo, intrarenal inhibition of gap junctional intercellular communication increases spatiotemporal fluctuation of cortical surface perfusion and impairs both dynamic and steady-state autoregulation of renal blood flow. This finding links synchronization of microcirculatory dynamics mediated by gap junctional intercellular communication to autoregulatory effectiveness.

Zebrafish heart as a model to study the integrative autonomic control of pacemaker function
Matthew R. Stoyek, T. Alexander Quinn, Roger P. Croll, Frank M. Smith
September 1, 2016: H676-H688
DOI: 10.1152/ajpheart.00330.2016

The intracardiac nervous system represents the final common pathway for autonomic control of pacemaker function. Here we establish the isolated zebrafish heart as a viable model for investigating this system and characterize a neurally mediated shift in pacemaker locus from the sinoatrial to the atioventricular region.

MicroRNA-140 is elevated and mitofusin-1 is downregulated in the right ventricle of the Sugen5416/hypoxia/normoxia model of pulmonary arterial hypertension.
Sachindra Raj Joshi, Vidhi Dhagia, Salina Gairhe, John G. Edwards, Ivan F. McMurtry, Sachin A. Gupte
September 1, 2016: H689-H698
DOI: 10.1152/ajpheart.00264.2016

We show that in an experimental model of severe pulmonary arterial hypertension, miR-140 is significantly upregulated in the hypertrophic right ventricle, and its target protein mitofusin-I is significantly downregulated. The increase in miR-140 is significantly correlated with increase in right ventricular systolic pressure and right ventricle hypertrophy.

Intermittent hypoxia and arterial blood pressure control in humans: role of the peripheral vasculature and carotid baroreflex
Exposure of healthy humans to 6 h of intermittent hypoxia appears to exert heterogeneous effects on the limb vasculature, with the lower limb being more vulnerable. Increased arterial stiffness and impaired sympathetic withdrawal may contribute to the upward shift of the carotid baroreflex facilitating intermittent hypoxia-induced development of hypertension.

Mitochondrial long noncoding RNAs as blood based biomarkers for cardiac remodeling in patients with hypertrophic cardiomyopathy
Janina Kitow, Anselm A. Derda, Regalla Kumarswarmy, Angelika Pfanne, Jasmin Fendrich, Johan M. Lorenzen, Ke Xiao, Udo Bavendiek, Johann Bauersachs, Thomas Thum
September 1, 2016: H707-H712
DOI: 10.1152/ajpheart.00194.2016

This study investigated remodeling and mitochondrial associated long noncoding RNAs being increased in blood of patients suffering from hypertrophic obstructive cardiomyopathy. Especially, long noncoding RNAs uc004cov.4 and uc022bqu.1 were able to identify these patients and may be used as clinical biomarkers in future.

Nitric oxide production contributes to Bacillus anthracis edema toxin-associated arterial hypotension and lethality: ex vivo and in vivo studies in the rat
Yan Li, Xizhong Cui, Wanying Xu, Lernik Ohanjanian, Hanish Sampath-Kumar, Dante Suffredini, Mahtab Moayeri, Stephen Leplla, Yvonne Fitz, Peter Q. Eichacker
September 7, 2016: H781-H793
DOI: 10.1152/ajpheart.00163.2016

The most important aspect of the present study is the finding that the hypotensive and lethal effects of Bacillus anthracis edema toxin are mediated in part via the production of nitric oxide (NO) and that coadministration of an NO synthase inhibitor with edema toxin challenge has a beneficial survival effect.

Effect of PEEP, blood volume, and inspiratory hold maneuvers on venous return
David Berger, Per W. Moller, Alberto Weber, Andreas Bloch, Stefan Bloechlinger, Matthias Haenggi, Soren Sondergaard, Stephan M. Jakob, Sheldon Magder, Jukka Takala
September 7, 2016: H794-H806
DOI: 10.1152/ajpheart.00931.2015

Enhanced recovery of inferior vena cava blood flow (QIVC) during inspiratory holds shifts the right atrial pressure/pulmonary artery blood flow relationship to the right. Hence, the mean systemic filling pressure obtained via extrapolation of pressure-flow relationships with airway occlusion overestimates the mean systemic filling pressure measured during right atrial balloon occlusion at end-expiratory lung volume. The preferential QIVC recovery helps to maintain venous return during sustained increased inspiratory airway pressure. The underlying mechanism is likely to be a hepatosplanchnic vascular waterfall.

Pregnancy mitigates cardiac pathology in a mouse model of left ventricular pressure overload
Hong Xu, Elza D. van Deel, Mark R. Johnson, Petra Opic, Bronwen R. Herbert, Els Moltzer, Suren R. Sooranna, Heleen van Beusekom, Wang-Fu Zang, Dirk J. Duncker, Jolien W. Roos-Hesselink
September 7, 2016: H807-H814
DOI: 10.1152/ajpheart.00056.2016

Little is known about the effect of pregnancy on heart disease. We found that aortic stenosis did not affect fetal outcome and that pregnancy, rather than exacerbating LV dysfunction, attenuated cardiac remodeling and mitigated pulmonary congestion and pathological gene expression, suggesting positive effects of pregnancy on the pressure-overloaded heart.

CXCL16 regulates renal injury and fibrosis in experimental renal artery stenosis
Zhiheng Ma, Xiaogao Jin, Liqun He, Yanlin Wang
September 7, 2016: H815-H821
DOI: 10.1152/ajpheart.00948.2015

Renal artery stenosis (RAS) is an important cause of chronic kidney disease. The underlying mechanisms are not well understood. Our study indicates that CXCL16 plays an important role in the pathogenesis of RAS-induced renal injury and fibrosis through regulation of myeloid fibroblast accumulation and inflammatory cell infiltration.

Defining the sham environment for post-myocardial infarction studies in mice
Rugmani Padmanabhan Iyer, Lisandra E. de Castro Brás, Presley L. Cannon, Yonggang Ma, Kristine Y. DeLeon-Pennell, Mira Jung, Elizabeth R.
Day 0 controls (mice with no surgical operation) can be a good substitute for sham surgeries in myocardial infarction studies, particularly for time course analyses that evaluate multiple time points.

**Muscle Mechanics and Ventricular Function**

*Myocardial reverse remodeling after pressure unloading is associated with maintained cardiac mechanoenergetics in a rat model of left ventricular hypertrophy*

Mihály Ruppert, Sevil Korkmaz-Icöz, Shiliang Li, Balázs Tamás Németh, Péter Hagedüsü, Paige Brlecic, Csaba Mátyás, Markus Zorn, Béla Merkely, Matthias Karck, Tamás Radovits, Gábor Szabó

September 1, 2016 : H592-H603

DOI: 10.1152/ajpheart.00085.2016

*Our experiment demonstrates for the first time that the regression of left ventricular hypertrophy by pressure unloading not only leads to preserved diastolic function, and reversed maladaptive contractility augmentation, but also to maintained cardiac mechanoenergetics. Therefore, pressure unloading at a relatively early time point could result in complete functional recovery.*

**Reversible redox modifications of ryanodine receptor ameliorate ventricular arrhythmias in the ischemic-reperfused heart**

Romina Becerra, Bárbara Román, Mariano Di Carlo, Juan Ignacio Mariangelo, Margarita Salas, Gina Sánchez, Paulina Donoso, Guillermo R. Schinella, Leticia Vittone, Xander H. Wehrens, Cecilia Mundíña-Weilenmann, Matilde Said

September 1, 2016 : H713-H724

DOI: 10.1152/ajpheart.00142.2016

*This study demonstrates that redox changes of ryanodine receptor type 2 occur together with Ca²⁺ calmodulin-dependent kinase II phosphorylation of the sarcoplasmic reticulum Ca²⁺ channel in hearts subjected to ischemia/reperfusion. Both posttranslational modifications seem to act synergistically in determining reperfusion arrhythmogenesis.*

**Signaling and Stress Response**

*Tyrosine kinase inhibitor BIBF1000 does not hamper right ventricular pressure adaptation in rats*

Michiel Alexander de Raaf, Franziska Elena Herrmann, Ingrid Schalij, Frances S. de Man, Anton Vonk-Noordegraaf, Christophe Guignabert, Lutz Wolfin, Harm Jan Bogaard

June 24, 2016 : H604-H612

DOI: 10.1152/ajpheart.00656.2015

*On the basis of this translational rat study, it is suggested that cardiac function will not worsen when nintedanib is used for treatment of idiopathic pulmonary fibrosis, even after the development of associated pulmonary hypertension.*

**Vascular Biology and Microcirculation**

*Increase of cortical cerebral blood flow and further cerebral microcirculatory effects of Serelaxin in a sheep model*

Sabine J. Bischoff, Martin Schmidt, Thomas Lehmann, Andrey Irintchev, Harald Schubert, Christian Jung, Matthias Schwab, Otmar Huber, Georg Matziolis, René Schifflner

September 1, 2016 : H613-H620

DOI: 10.1152/ajpheart.00118.2016

*Using laser Doppler flowmetry and sidestream dark-field imaging techniques, we show that Serelaxin induces an increase of cortical, but not subcortical, cerebral microcirculation after an intravenous bolus injection in a sheep model. Relaxin receptor RXFP1 is expressed in the respective brain regions and may mediate the effects.*

*4D intravital microscopy uncovers critical strain differences for the roles of PECAM and CD99 in leukocyte diapedesis*

David P. Sullivan, Richard L. Watson, William A. Muller

September 1, 2016 : H621-H632

DOI: 10.1152/ajpheart.00289.2016

*The data presented in this study help clarify seemingly discrepant findings in the field involving two of the common mouse strains used to study inflammation, particularly regarding the roles of PECAM and CD99 in leukocyte transendothelial migration.*
Short fungal fractions of β-1,3 glucans affect platelet activation
Hélène Vancraeynest, Rogatien Charlet, Yann Guerardel, Laura Chateau, Anne Bauters, Meryem Tardivel, Nadine François, Laurent Dubuquoy, Dmitry Soloviev, Daniel Poulain, Boualem Sendid, Samir Jawhara
September 1, 2016 : H725-H734
DOI: 10.1152/ajpheart.00907.2015

Our study shows that the soluble short fractions of β-1,3 glucans act as a shield for Candida albicans. These fractions reduce platelet-neutrophil interactions, and platelet activation through TLR4-mediated TGF-β1 production and ATP release, and blocking this receptor by an anti-TLR4 antibody abolished the effect of the pentaglucosides on platelets.

Identification of human sympathetic neurovascular control using multivariate wavelet decomposition analysis
Saqib Saleem, Paul D. Teal, W. Bastiaan Kleijn, Philip N. Ainslie, Yu-Chieh Tzeng
September 7, 2016 : H837-H848
DOI: 10.1152/ajpheart.00254.2016

The sympathetic nervous system plays an important role in blood pressure control, but whether it is involved in cerebral blood flow regulation remains controversial. Here we applied wavelet decomposition analysis and found that sympathetic activity is a powerful determinant of very-low-frequency fluctuations in cerebral blood flow.

Rapid Report

Local renin-angiotensin system mediates endothelial dilator dysfunction in aging arteries
Sheila Flavahan, Fumin Chang, Nicholas A. Flavahan
September 7, 2016 : H849-H854
DOI: 10.1152/ajpheart.00422.2016

The study demonstrates for the first time that the impaired activity of endothelial nitric oxide-dependent dilatation in aging arteries is mediated by a local renin-angiotensin system and pathological signaling of angiotensin II. Inhibition of angiotensin synthesis or activity in isolated arteries rapidly and completely restores normal endothelial dilatation in old arteries.

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Role of mesothelin in carbon nanotube-induced carcinogenic transformation of human bronchial epithelial cells
Xiaoqing He, Emily Despeaux, Todd A. Stueckle, Alexander Chi, Vincent Castranova, Cerasela Zoica Dinu, Liying Wang, Yon Rojanasakul
September 1, 2016: L538-L549
DOI: 10.1152/ajplung.00139.2016

Influences of innate immunity, autophagy, and fibroblast activation in the pathogenesis of lung fibrosis
David N. O'Dwyer, Shanna L. Ashley, Bethany B. Moore
September 1, 2016: L590-L601
DOI: 10.1152/ajplung.00221.2016

Identification of genes differentially regulated by vitamin D deficiency that alter lung pathophysiology and inflammation in allergic airways disease
Rachel E. Foong, Anthony Bosco, Niamh M. Troy, Shelley Gorman, Prue H. Hart, Anthony Kicic, Graeme R. Zosky
September 13, 2016: L653-L663
DOI: 10.1152/ajplung.00026.2016

Restoration of R117H CFTR folding and function in human airway cells through combination treatment with VX-809 and VX-770
Martina Gentzsch, Hong Y. Ren, Scott A. Houck, Nancy L. Quinney, Deborah M. Cholon, Pattarawut Sopha, Imron G. Chaudhry, Jhuma Das, Nikolay V. Dokholyan, Scott H. Randell, Douglas M. Cyr
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DOI: 10.1152/ajplung.00186.2016

Endothelial hyperpermeability in severe pulmonary arterial hypertension: role of store-operated calcium entry
Chun Zhou, Mary I. Townsley, Mikhail Alexeyev, Norbert F. Voelkel, Troy Stevens
September 1, 2016: L560-L569
DOI: 10.1152/ajplung.00057.2016

Cigarette smoke causes acute airway disease and exacerbates chronic obstructive lung disease in neonatal mice
Jie Jia, Thomas M. Conlon, Carolina Ballester Lopez, Michael Seimetz, Mariola Bednorz, Zhe Zhou-Suckow, Norbert Weissmann, Oliver Eickelberg, Marcus A. Mall, Ali Onder Yildirim
September 1, 2016: L602-L610
DOI: 10.1152/ajplung.00124.2016

Staphylococcus aureus α-toxin-mediated cation entry depolarizes membrane potential and activates p38 MAP kinase in airway epithelial cells
Ina Eiffler, Jane Behnke, Sabine Ziesemer, Christian Müller, Jan-Peter Hildebrandt
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DOI: 10.1152/ajplung.00090.2016

Loss of CCR2 signaling alters leukocyte recruitment and exacerbates γ-herpesvirus-induced pneumonitis and fibrosis following bone marrow transplantation
Stephen J. Gurczynski, Megan C. Procario, David N. O'Dwyer, Carol A. Wilke, Bethany B. Moore
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DOI: 10.1152/ajplung.00193.2016

GABA_A- and glycine-mediated inhibitory modulation of the cough reflex in the caudal nucleus tractus solitarii of the rabbit
Elenia Cinelli, Ludovica Iovino, Fulvia Bongianni, Tito Pantaleo, Donatella Mutolo
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Dendritic cells induce Te1 cell differentiation via the CD40/CD40L pathway in mice after exposure to cigarette smoke
Liang-Jian Kuang, Ting-Ting Deng, Qin Wang, Shi-Lin Qiu, Yi Liang, Zhi-Yi He, Jian-Quan Zhang, Jing Bai, Mei-Hua Li, Jing-Min Deng, Guang-Nan Liu, Ji-Feng Liu, Xiao-Ning Zhong
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Boysenberry ingestion supports fibrolytic macrophages with the capacity to ameliorate chronic lung remodeling
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In vitro and in vivo evidence for an inflammatory role of the calcium channel TRPV4 in lung epithelium: Potential involvement in cystic fibrosis
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DOI: 10.1152/ajplung.00442.2015

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The pluralization of septum
Rory E. Morty
September 13, 2016 : L686
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Call for Papers | Sex and Gender: Differences in Cardiovascular, Renal, and Metabolic Diseases

Sex differences in the cardiovascular consequences of the inspiratory muscle metaboreflex
Joshua R. Smith, Ryan M. Broxterman, Shane M. Hammer, Andrew M. Alexander, Kaylin D. Didier, Stephanie P. Kurti, Thomas J. Barstow, Craig A. Harms
September 9, 2016 : R574-R581
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Highly sensitive index of sympathetic activity based on time-frequency spectral analysis of electrodermal activity
Hugo F. Posada-Quintero, John P. Florian, Alvaro D. Orjuela-Cañón, Ki H. Chon
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Neural Control

Hypernatremia-induced vasopressin secretion is not altered in TRPV1−/− rats
Andrew Blake Tucker, Sean D. Stocker
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DOI: 10.1152/ajpregu.00483.2015

Ventral tegmental area orexin 1 receptors promote palatable food intake and oppose postigestive negative feedback
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Andrew Blake Tucker, Sean D. Stocker
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Hydrogen sulfide contributes to hypoxic inhibition of airway transepithelial sodium absorption
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Alex G. Little, Frank Seebacher
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Oxidized fish oil in rat pregnancy causes high newborn mortality and increases maternal insulin resistance
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Minglin Zhu, Zongli Ren, José S. Possomato-Vieira, Raouf A. Khalil
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Osmotically inactive sodium and potassium storage: lessons learned from the Edelman and Boling data
Minhtri K. Nguyen, Dai-Scott Nguyen, Minh-Kevin Nguyen
September 1, 2016  F539-F547
Measurement of voluntary activation based on transcranial magnetic stimulation over the motor cortex
Gabrielle Todd, Janet L. Taylor, Simon C. Gandevia
September 1, 2016: 678-686
DOI: 10.1152/japplphysiol.00708.2016

Differential effects of respiratory and electrical stimulation-induced dilator muscle contraction on mechanical properties of the pharynx in the pig
A. Brodsky, Y. Dotan, M. Samri, A. R. Schwartz, A. Oliven
September 1, 2016: 606-614
DOI: 10.1152/japplphysiol.00783.2015

Respiratory stimulation and electrical stimulation of the hypoglossus nerve differ in the mechanism by which they stabilize the pharynx in the isolated upper airway of the pig: respiratory stimulation reduces pharyngeal compliance, i.e., stiffens the area of collapse, whereas electrical stimulation lowers extrapharyngeal pressure, as calculated from the area-pressure curve. Tongue muscles, but not the neck muscles and thoracic forces, contributed to the respiratory stimulation-induced stiffening of the pharynx in this study.

Evaluating the control: minipump implantation and breathing behavior in the neonatal rat
Ian J. Kidder, Jordan A. Mudery, Santiago Barreda, David J. Taska, E. Fiona Bailey
September 1, 2016: 615-622
DOI: 10.1152/japplphysiol.00080.2016

Accumulating evidence indicates that gestational and/or neonatal stress perturbs central nervous system (CNS) development and that fetal exposure to anesthetic agents or narcotics disrupts critical processes of axonal growth and synapse elimination. Here we focus on processes related to minipump implantation surgery and the potential impact of implant surgery on early postnatal respiratory control and function.

Exercise physiological responses to drug treatments in chronic thromboembolic pulmonary hypertension
September 1, 2016: 623-628
DOI: 10.1152/japplphysiol.00087.2016

This is the first study using gas exchange during exercise to assess the response to pulmonary arterial hypertension drug therapy in patients with chronic thromboembolic pulmonary hypertension. We also for the first time compare patients with operable and inoperable chronic thromboembolic pulmonary hypertension.

Prolonged adenosine triphosphate infusion and exercise hyperemia in humans
John R. A. Shepherd, Michael J. Joyner, Frank A. Dinennon, Timothy B. Curry, Sushant M. Ranadive
September 1, 2016: 629-635
DOI: 10.1152/japplphysiol.01034.2015

The novel and noteworthy findings are 1) in humans, the vasodilator response to infusion of exogenous ATP does not wane and 2) the magnitude of change in hyperemic responses to exercise during the ATP infusion is unaffected. The ability of ATP to evoke prolonged vasodilation shows it meets a key criterion of any putative dilator substance. The latter observation suggests a disconnect between the usual matching of blood flow and oxygen delivery during contractions.

Maximal oxygen uptake is proportional to muscle fiber oxidative capacity, from chronic heart failure patients to professional cyclists
Stephan van der Zwaard, C. Jo de Ruiter, Dionne A. Noordhof, Renske Sterrenburg, Frank W. Bloemers, Jos J. de Koning, Richard T. Jaspers, Willem J. van der Laarse
September 1, 2016: 636-645
DOI: 10.1152/japplphysiol.00355.2016

Maximal oxygen uptake during whole body exercise is presumably constrained by oxygen delivery to mitochondria rather than by mitochondria's ability to consume oxygen. However, mitochondrial oxidative overcapacity remains unclear due to complicated isolation and permeabilization procedures. In the present study, human maximal oxygen uptake attained during cycling exercise is related and 90% of mitochondrial oxidative capacity predicted from skeletal muscle succinate dehydrogenase activity. This mitochondrial oxidative overcapacity is substantially lower than
Morphological and molecular aspects of immobilization-induced muscle atrophy in rats at different stages of postnatal development: the role of autophagy
Camila Silva Foresto, Silvia Paula-Gomes, Wilian Assis Silveira, Flávia Aparecida Graça, Isis do Carmo Ketelhut, Dawit Albieiro Pinheiro Gonçalves, Ana Claudia Mattiello-Sverzut
September 1, 2016 : 646-660
DOI: 10.1152/japplphysiol.00687.2015

Immobilization induces muscle maladaptations at different stages of postnatal development, but the cellular mechanisms involved in such effects are unclear. Our data show that the alterations in muscle proteostasis during immobilization occur in age-independent and -dependent manners and muscle disorders are aggravated by autophagy blockade with colchicine, inducing a myopathic profile. This understanding may help us optimize treatment outcomes in immobilized adults and infants and encourages the testing of different autophagy inhibitors in muscle atrophy.

Dietary nitrate supplementation: impact on skeletal muscle vascular control in exercising rats with chronic heart failure
Scott K. Ferguson, Clark T. Holdsworth, Trenton D. Colburn, Jennifer L. Wright, Jesse C. Craig, Alex Fees, Andrew M. Jones, Jason D. Allen, Timothy I. Musch, David C. Poole
September 1, 2016 : 661-669
DOI: 10.1152/japplphysiol.00014.2016

Chronic heart failure (CHF) impairs skeletal muscle vascular control and tolerance to exercise. Dietary nitrate supplementation elevates skeletal muscle blood flow and improves exercise performance in some populations. Here we demonstrate that nitrate supplementation via beetroot juice elevates skeletal muscle blood flow during exercise in rats with moderate CHF.

Intermittent hypoxia induces murine macrophage foam cell formation by IKK-β-dependent NF-κB pathway activation
Toshihiro Imamura, Orit Poulsen, Gabriel G. Haddad
September 1, 2016 : 670-677
DOI: 10.1152/japplphysiol.00307.2016

Intermittent hypoxia (IH)-induced inflammation increases the risk of atherosclerosis in obstructive sleep apnea (OSA) patients. However, the effect of IH on macrophage foam cell formation, a key player in atherosclerosis, has not been elucidated. We demonstrate for the first time that IH-induced foam cell formation is diminished by IKK-β deletion. Our findings highlight the importance of the IKK-β-dependent NF-κB pathway and the potential of this pathway as a therapeutic target.

Fibroblast growth factor 21 is required for beneficial effects of exercise during chronic high-fat feeding
Christine Loyd, I. Jack Magrisso, Michael Haas, Sowmya Balusu, Radha Krishna, Nobuyuki Itoh, Darleen A. Sandoval, Diego Perez-Tilve, Silvana Obici, Kirk M. Habegger
September 1, 2016 : 687-698
DOI: 10.1152/japplphysiol.00456.2016

Home-based aerobic exercise training improves skeletal muscle oxidative metabolism in patients with metabolic myopathies
Simone Porcelli, Mauro Marzorati, Lucia Morandi, Bruno Grassi
September 1, 2016 : 699-708
DOI: 10.1152/japplphysiol.00885.2015

Twelve weeks of home-based moderate-intensity aerobic training in mitochondrial myopathies and McArdle's disease patients attenuated the impairments of skeletal muscle oxidative metabolism and improved variables associated with exercise tolerance. Despite this, 3-mo after the termination of the exercise training program the level of habitual physical activity was not increased vs. the baseline.

Pregnancy at high altitude in the Andes leads to increased total vessel density in healthy newborns
Norina N. Gassmann, Hugo A. van Elteren, Tom G. Goos, Claudia R. Morales, Maria Rivera-Ch, Daniel S. Martin, Patricia Cabala Peralta, Agustin Passano del Carpio, Saul Aranibar Machaca, Luis Huicho, Irwin K. M. Reiss, Max Gassmann, Rogier C. J. de Jonge
September 1, 2016 : 709-715
DOI: 10.1152/japplphysiol.00561.2016

The natural hypoxic environment at high altitude results in reduced oxygenation, especially in the growing human fetus. Our prospective observational study on healthy term newborns in Peru (Puno at 3,840 m) that included novel noninvasive visualization of microcirculation demonstrates that vessel density is elevated by 14% in neonates born to women living at high altitude compared with babies born at sea level, most likely revealing an early adaptive mechanism to a highly hypoxic antenatal environment.

Passive heat therapy improves cutaneous microvascular function in sedentary humans via improved nitric oxide-dependent dilation
We showed for the first time that passive heat therapy improves cutaneous microvascular function in humans via improved nitric oxide (NO)-dependent dilation. This is the first study to investigate the mechanisms underlying improvements in vascular health associated with heat therapy. Our data add to the currently limited but strong evidence suggesting heat therapy could be a powerful novel tool for improving cardiovascular health, particularly in disease states characterized by impaired vascular function secondary to reduced NO bioavailability.

No difference in exogenous carbohydrate oxidation during exercise in children with and without impaired glucose tolerance
Lisa Chu, Katherine M. Morrison, Michael C. Riddell, Sandeep Raha, Brian W. Timmons
September 1, 2016 : 724-729
DOI: 10.1152/japplphysiol.00419.2016
This article is the first to report exogenous carbohydrate oxidative efficiency during exercise in children with impaired glucose tolerance using $^{13}$C-stable isotope methodology. The capacity to utilize exogenous carbohydrate was not impaired in children with impaired glucose tolerance compared with normal glucose tolerance, despite lower insulin sensitivity and beta-cell function. The findings suggest that exogenous carbohydrate oxidation was maintained during exercise, possibly via endocrine compensatory responses, such as increased insulin secretion, or via non-insulin-mediated mechanisms.

Effect of betamethasone, surfactant, and positive end-expiratory pressures on lung aeration at birth in preterm rabbits
Jessica R. Crawshaw, Stuart B. Hooper, Arjan B. te Pas, Beth A. Allison, Megan J. Wallace, Lauren T. Kerr, Robert A. Lewis, Colin J. Morley, Andrew F. Leong, Marcus J. Kitchen
September 1, 2016 : 750-759
DOI: 10.1152/japplphysiol.01043.2015
Antenatal betamethasone, surfactant therapy, and positive end-expiratory pressure (PEEP) ventilation are frequently used in combination to improve lung function in preterm newborns. However, it is unclear how these factors interact to enhance functional residual capacity (FRC) and dynamic lung compliance (CDL) at birth. Contrary to expectation, betamethasone hindered FRC development and abolished the benefit of low PEEP, yet improved CDL. However, surfactant administration counteracted the adverse effect of betamethasone on FRC recruitment at birth.

Human motor control of landing from a drop in simulated microgravity
C. N. Gambelli, D. Theisen, P. A. Willems, B. Scheepens
September 1, 2016 : 760-770
DOI: 10.1152/japplphysiol.00305.2016
For the first time, the control of landing from a jump and from a drop is compared in weightlessness with different simulated gravity conditions (1–0.2 g). In these unusual conditions, humans adjust the landing command according to the amount of energy to be dissipated. Kinetic, kinematic, and electromyographic observations contribute to understanding the underlying mechanisms through which the central nervous system plans a complex motor task.

Effects of pacing modality on noninvasive assessment of heart rate dependency of indices of large artery function
Isabella Tan, Hosen Kiat, Edward Barin, Mark Butlin, Alberto P. Avolio
September 1, 2016 : 771-780
DOI: 10.1152/japplphysiol.00445.2016
This was the first study to demonstrate significant differences in wave reflection indices with different cardiac pacing modalities. This has implications for future heart rate studies in wave reflections, and studies should either be designed to employ a single pacing modality for inducing heart rate changes, or to take pacing modality into account in the analysis.

Membrane progesterone receptor-β, but not -α, in dorsal brain stem establishes sex-specific chemoreflex responses and reduces apnea frequency in adult mice
Ryma Boukari, Orlane Rossignol, Cécile Baldy, François Marcouiller, Aida Bairam, Vincent Joseph
September 1, 2016 : 781-791
DOI: 10.1152/japplphysiol.00397.2016
We tested the hypothesis that membrane progesterone receptors (mPR) contribute to respiratory control in adult male and female mice. The main results show that reduced expression of mPRβ (achieved by intracerebroventricular treatment with small interfering RNA) increases (3×) the frequency of apnea, suppresses the chemoreflex response to hypoxia, and reduces the response to hypercapnia. By contrast, mPRα had limited effects, slightly reducing the ventilatory response to hypercapnia.

Testosterone inhibits expression of lipogenic genes in visceral fat by an estrogen-dependent mechanism
Combined effects of resistance training and calorie restriction on mitochondrial fusion and fission proteins in rat skeletal muscle
Yu Kitaoka, Koichi Nakazato, Riki Ogasawara
September 1, 2016 : 806-810
DOI: 10.1152/japplphysiol.00465.2016

The original aim of this study was to examine the effects of resistance training with calorie restriction on skeletal muscle adaptation. We found that calorie restriction enhanced resistance training-induced increases in protein levels of peroxisome proliferator-activated receptor-γ coactivator-1α, and in proteins involved in mitochondrial fusion (Opa1 and Mfn1) and oxidative phosphorylation.

Presence of dipalmitoylphosphatidylcholine from the lungs at the active hydrophobic spots in the vasculature where bubbles are formed on decompression
Ran Arieli, Soliman Khatib, Jacob Vaya
September 1, 2016 : 811-815
DOI: 10.1152/japplphysiol.00649.2016

Lipopolysaccharide exposure during the early postnatal period adversely affects the structure and function of the developing rat carotid body
Zankhana R. Master, Andrea Porzionato, Kalpashri Kesavan, Ariel Mason, Raul Chavez-Valdez, Machiko Shirahata, Estelle B. Gauda
September 1, 2016 : 816-827
DOI: 10.1152/japplphysiol.01094.2015

We have developed a newborn animal model of spontaneous intermittent hypoxia. Exposure to LPS during early postnatal development in rat pups significantly increases spontaneous intermittent desaturations and decreases the ventilatory and carotid sinus nerve responses to hypoxia that persist for 1 wk after exposure. Our model may simulate the chronic intermittent hypoxia that is often seen in premature infants with perinatal inflammation and help to further delineate mechanisms leading to disordered breathing in premature infants.

HIGHLIGHTED TOPIC | Molecular Adaptations to Exercise, Heat Acclimation, and Thermotolerance

The role of Nrf2 in skeletal muscle contractile and mitochondrial function
Matthew J. Crilly, Liam D. Tryon, Avigail T. Erlich, David A. Hood
September 1, 2016 : 730-740
DOI: 10.1152/japplphysiol.00042.2016

Nrf2 is critical for mediating an antioxidant defense against oxidative insults. Emerging evidence has implicated Nrf2 in the regulation of mitochondrial function in some cell types, but no research has been devoted to understanding its contribution to exercise performance and mitochondrial biogenesis in muscle. Our work is the first to show that the presence of Nrf2 has an impact on muscle endurance performance and mitochondrial function in skeletal muscle.

Transcriptional control, but not subcellular location, of PGC-1α is altered following exercise in a hot environment
Matthew W. Heesch, Robert J. Shute, Jodi L. Kreiling, Dustin R. Slivka
September 1, 2016 : 741-749
DOI: 10.1152/japplphysiol.01065.2015

This investigation explores the transcriptional control and subcellular location of proliferator-activated receptor-γ coactivator 1-α (PGC-1α) following exercise in a hot environment. It provides new evidence for decreased transcription of PGC-1α following an acute exercise bout in a hot environment, coinciding with decreased binding of cAMP response element-binding protein (CREB), myocyte enhancer factor 2 (MEF2), and forkhead box class-O1 (FoxO1) to the PGC-1α promoter region. However, translocation of PGC-1α protein from the cytosol into the nucleus following exercise appears to be unaffected by differences in environmental temperature.

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Neuro Forum

Cerebellar role in Parkinson's disease

Jasmine L. Mirdamadi
September 1, 2016 : 917-919

DOI: 10.1152/jn.01132.2015

Review

Cognitive dysfunction in Duchenne muscular dystrophy: a possible role for neuromodulatory immune molecules

Mark G. Rae, Dervla O'Malley
September 1, 2016 : 1304-1315

DOI: 10.1152/jn.00248.2016

CALL FOR PAPERS | Active Sensing

Active sensing without efference copy: referent control of perception

Anatol G. Feldman
September 1, 2016 : 960-976

DOI: 10.1152/jn.00016.2016

The notions of direct neural preprogramming of the motor outcome and the use of a copy of commands to muscles (efference copy) to control our senses conflict with basic physiological and physical principles. Instead, the brain predetermines where, in the spatial domain, muscles can work whereas commands to muscles emerge in this domain due to the interaction of the neuromuscular system with the environment, thus solving several problems in action and perception.

Reduced frontal theta oscillations indicate altered crossmodal prediction error processing in schizophrenia

Yadira Roa Romero, Julian Keil, Johanna Balz, Jürgen Gallinat, Daniel Senkowski
September 1, 2016 : 1396-1407

DOI: 10.1152/jn.00096.2016

We examined the neural correlates of crossmodal prediction error in audiovisual speech in schizophrenia. Interestingly, we found intact audiovisual incongruence detection in the auditory cortex for patients with schizophrenia (SZP) and healthy matched control participants (HC). However, we found that the enhanced frontal theta-band power, which reflects crossmodal prediction error processing in HC, was absent in SZP.

CALL FOR PAPERS | Auditory System Plasticity

Effect of current focusing on the sensitivity of inferior colliculus neurons to amplitude-modulated stimulation

Shefin S. George, Mohit N. Shivdasani, James B. Fallon
September 1, 2016 : 1104-1116

DOI: 10.1152/jn.00126.2016

In this study, we explored the capability of inferior colliculus neurons to detect amplitude-modulated cochlear implant stimulation with current focusing stimulation compared with monopolar stimulation. To our knowledge, the data presented represent the first report of electrophysiological modulation detection using focused multipolar and tripolar stimulation.

CALL FOR PAPERS | Building Neural Circuits: Wiring and Experience

Spontaneous activity and functional connectivity in the developing cerebellerubral system

Carlos Del Rio-Bermudez, Alan M. Plumeau, Nicholas J. Sattler, Greta Sokoloff, Mark S. Blumberg
September 1, 2016 : 1316-1327

DOI: 10.1152/jn.00461.2016
Investigations of functional development in cerebellar networks can inform our understanding of the origins of neurodevelopmental disorders such as schizophrenia and autism. Critical to the function of these networks is the cerebellorubral pathway, which connects the cerebellum with one of its primary efferent targets, the red nucleus. For the first time, we characterize sleep- and wake-related neural activity in this critical system in infant rats during a period of rapid developmental change.

**CALL FOR PAPERS | Comparative Approaches in Neurobiology**

**Mechanisms of spreading depolarization in vertebrate and insect central nervous systems**
Kristin E. Spong, R. David Andrew, R. Meldrum Robertson
September 1, 2016 : 1117-1127

DOI: 10.1152/jn.00352.2016

Spreading depolarization in the brain of *Drosophila* is induced by inhibition of the Na⁺/K⁺-ATPase and mitigated by a decrease in activity of protein kinase G
Kristin E. Spong, Esteban C. Rodriguez, R. Meldrum Robertson
September 1, 2016 : 1152-1160

DOI: 10.1152/jn.00353.2016

We have developed an experimental protocol that allows us reliably to induce and monitor spreading depolarization (SD) in the brain of the fruit fly, opening the way for a wide range of powerful molecular genetic techniques to target specific processes in specific tissues. With the use of our fly model, we provide evidence that the protein kinase G pathway, which has been conserved through evolution, is a potential molecular target to reduce brain susceptibility to SD.

**CALL FOR PAPERS | Control of Autonomic Function: Insights from Neurophysiological Studies in Conscious Animals (Including Humans)**

**“Real-time” imaging of cortical and subcortical sites of cardiovascular control: concurrent recordings of sympathetic nerve activity and fMRI in awake subjects**
September 1, 2016 : 1199-1207

DOI: 10.1152/jn.00783.2015

**CALL FOR PAPERS | Methods to Understand Brain Connections and Neural Function**

**Brain heating induced by near-infrared lasers during multiphoton microscopy**
Kaspar Podgorski, Gayathri Ranganathan
September 1, 2016 : 1012-1023

DOI: 10.1152/jn.00275.2016

New optical tools are transforming neuroscience, allowing increasingly comprehensive control and readout of neural circuits. However, emerging parallel microscopy methods rely on higher total illumination powers than conventional techniques, raising concerns about heating and its effects on the brain. This study characterizes these effects under serial and parallel illumination schemes, allowing researchers to predict power limits for their experiments. Even under serial illumination, usable power can be limited by heating rather than nonlinear damage.

**Optogenetic manipulation of neural circuits in awake marmosets**
Matthew MacDougall, Samuel U. Nummela, Shanna Coop, Anita Disney, Jude F. Mitchell, Cory T. Miller
September 1, 2016 : 1286-1294

DOI: 10.1152/jn.00197.2016

Marmosets have emerged as a valuable model for applying modern molecular techniques to the study of the primate brain. We developed a novel, chronic preparation for optogenetic photostimulation of cortical neurons in awake marmosets. This approach is well suited for use in studies aimed at investigating functional neural circuitry in behaving marmosets.

**CALL FOR PAPERS | Neurophysiology of Tactile Perception: A Tribute to Steven Hsiao**

**Neural mechanisms of selective attention in the somatosensory system**
Manuel Gomez-Ramirez, Kristjana Hysaj, Ernst Niebur
September 1, 2016 : 1218-1231

DOI: 10.1152/jn.00637.2015
CALL FOR PAPERS | Spinal Control of Motor Output

Self-reinnervated muscles lose autogenic length feedback, but intermuscular feedback can recover functional connectivity
Mark A. Lyle, Boris I. Prilutsky, Robert J. Gregor, Thomas A. Abelew, T. Richard Nichols
September 1, 2016 : 1055-1067
DOI: 10.1152/jn.00335.2016

Whereas autogenic length feedback is lost and contributes to motor deficits after muscle self-reinnervation, there is little known about the fate of intermuscular spinal circuitry. This study provides new evidence that despite permanent loss of the stretch reflex, intermuscular length and force feedback was preserved in most interactions tested. These findings support the hypothesis that recovered intermuscular circuitry could contribute to functional adaptations observed after peripheral nerve cut and repair.

Adaptive muscle plasticity of a remaining agonist following denervation of its close synergists in a model of complete spinal cord injury
Charline Dambreville, Jérémie Charest, Yann Thibaudier, Marie-France Hurteau, Victoria Kuczynski, Guillaume Grenier, Alain Frigon
September 1, 2016 : 1366-1374
DOI: 10.1152/jn.00328.2016

We show for the first time that the motor system caudal to a complete spinal cord injury can drive adaptive muscle plasticity in response to a peripheral nerve injury. This finding highlights the remarkable adaptive capacity of the lower levels of the systems controlling movement.

Upslope treadmill exercise enhances motor axon regeneration but not functional recovery following peripheral nerve injury
Jill Cannoy, Sam Crowley, Allen Jarratt, Kelly LeFevere Werts, Krista Osborne, Sohee Park, Arthur W. English
September 1, 2016 : 1408-1417
DOI: 10.1152/jn.00129.2016

In this paper, we investigated an increase on the dose of exercise used to promote the enhancement of axon regeneration and functional recovery following peripheral nerve injury. The more strenuous exercise of walking an upwardly sloped treadmill resulted in enhanced regeneration of motor axons and muscle reinnervation, but functional recovery was poorer than found using exercise on a level treadmill or no exercise at all.

Cellular and Molecular Properties of Neurons

Octopamine stabilizes conduction reliability of an unmyelinated axon during hypoxic stress
T. G. A. Money, M. K. J. Sproule, K. P. Cross, R. M. Robertson
September 1, 2016 : 949-959
DOI: 10.1152/jn.00354.2016

Neuronal signaling is energetically expensive, but the cost can be reduced by modulating action potential parameters to trade off performance against energy expenditure. We demonstrate that octopamine reverses some of the effects of hypoxia on axonal conduction of an important visual interneuron (DCMD) in locusts, thus maintaining its high conduction velocity at high firing frequencies. Pharmacological modulation of anoxic comas in intact animals suggests that octopamine has a general effect to enhance neural performance during hypoxia.

Using melanopsin to study G protein signaling in cortical neurons
K. M. McGregor, C. Bécamel, P. Marin, R. Andrade
September 1, 2016 : 1082-1092
DOI: 10.1152/jn.00406.2016

In this study melanopsin was transfected into pyramidal cells of the cerebral cortex to study G protein signaling in these cells with high temporal resolution.

Purkinje cell intrinsic excitability increases after synaptic long term depression
Zhen Yang, Fidel Santamaria
September 1, 2016 : 1208-1217
DOI: 10.1152/jn.00369.2016

Memory storage in Purkinje cells is assumed to be done by changing the strength of their synapses. Here, we show that a type of synaptic plasticity in Purkinje cell synapses results in an increase in the propensity of the cell to generate action potentials, known as intrinsic excitability. Since Purkinje cells are the output of the cerebellar cortex, this type of plasticity is expected to affect the information being sent to other parts of the brain.

Control of Homeostasis
In vitro characterization of noradrenergic modulation of chemosensitive neurons in the retrotrapezoid nucleus
Fu-Shan Kuo, Bárbara Falquetto, Dawei Chen, Luiz M. Oliveira, Ana C. Takakura, Daniel K. Mulkey
September 1, 2016 : 1024-1035
DOI: 10.1152/jn.00022.2016

Chemosensitive neurons in the retrotrapezoid nucleus (RTN) provide a CO₂/H⁺-dependent drive to breathe. Here, we show that norepinephrine (NE) differentially modulates activity of subsets of chemosensitive RTN neurons by α₁- and α₂-adrenergic receptor-dependent mechanisms. These results identify key components of the mechanism by which NE modulates activity of RTN chemoreceptors and suggest that there is a degree of neuromodulatory specialization among RTN chemoreceptors that may correlate with function.

α₁- and α₂-adrenergic receptors in the retrotrapezoid nucleus differentially regulate breathing in anesthetized adult rats
Luiz M. Oliveira, Thiago S. Moreira, Fu-Shan Kuo, Daniel K. Mulkey, Ana C. Takakura
September 1, 2016 : 1036-1048
DOI: 10.1152/jn.00023.2016

Disruption of norepinephrine signaling contributes to respiratory problems associated with disease states such as Rett syndrome. The presence of catecholaminergic varicosities is observed in the retrotrapezoid nucleus (RTN), a ventrolateral medullary region that contributes to central chemoreception and breathing. This study demonstrates that activation of RTN α₁- and α₂-adrenergic receptors leads to activation and inhibition of breathing, respectively, and the main source of catecholaminergic inputs to RTN is from the A7 region.

Glutamatergic drive facilitates synaptic inhibition of dorsal vagal motor neurons after experimentally induced diabetes in mice
Carie R. Boychuk, Bret N. Smith
September 1, 2016 : 1498-1506
DOI: 10.1152/jn.00325.2016

Results show that GABAergic synaptic regulation of central vagal motor neurons, which are responsible for regulating systemic energy homeostasis, undergoes complex functional reorganization in a type 1 diabetes model, including both glutamate-dependent and -independent forms of plasticity. These findings suggest a reorganization of brain stem circuitry regulating vagal motor output after several days of hyperglycemia/hypoinsulinemia that arises from, and could contribute to, visceral autonomic dysregulation in diabetes.

Control of Movement

Decisions in motion: vestibular contributions to saccadic target selection
September 1, 2016 : 977-985
DOI: 10.1152/jn.01071.2015

The neural mechanisms of decision making for actions have been studied extensively, but mostly when the subject is stationary. Our results directly examine decision-making in a dynamic environment, i.e., when the subject is in motion. Findings emphasize the impact of vestibular information on decision making, extending the importance of this sensory modality beyond its known role in reflexive responses and spatial orientation and opening up new avenues for neurophysiological investigations.

Startle reveals decreased response preparatory activation during a stop-signal task
Neil M. Drummond, Erin K. Cressman, Anthony N. Carlsen
September 1, 2016 : 986-994
DOI: 10.1152/jn.00216.2016

In this study a startling acoustic stimulus (SAS) was used to probe preparatory activation during a stop-signal task. Results indicated that although the response was prepared in advance during a stop-signal task, reaction time (RT) was delayed for both control and SAS trials compared with a simple RT task. The increased RT typically observed in a stop-signal task is therefore attributed to a reduced level of preparatory activation associated with the possibility of having to inhibit the response.

Distinct contributions of explicit and implicit memory processes to weight prediction when lifting objects and judging their weights: an aging study
Kevin M. Trewartha, J. Randall Flanagan
September 1, 2016 : 1128-1136
DOI: 10.1152/jn.01051.2015

Distinct memory processes underlie weight predictions used when lifting objects and making perceptual judgments about weight. However, the nature of these memory processes has yet to be revealed. By comparing the adaptability of weight predictions in younger and older adults our findings demonstrate that distinct neural mechanisms for declarative and nondeclarative memory processes are recruited when predicting object weight for the purpose of lifting objects and judging object weight, respectively.
Ampakine CX717 potentiates intermittent hypoxia-induced hypoglossal long-term facilitation
September 1, 2016 : 1232-1238
DOI: 10.1152/jn.00210.2016

The emerging interest in intermittent hypoxia as an adjunct to conventional neurorehabilitation strategies led us to examine if pharmacologic modulation of AMPA currents could enhance the respiratory motor response to intermittent hypoxia. In particular, this work focused on a class of drugs known as ampakines. Using a mouse model, we found that under appropriate conditions ampakine pretreatment can potentiate intermittent hypoxia-induced long-term facilitation of inspiratory burst amplitude recorded in the hypoglossal nerve.

Effect of coordinate frame compatibility on the transfer of implicit and explicit learning across limbs
Eugene Poh, Timothy J. Carroll, Jordan A. Taylor
September 1, 2016 : 1239-1249
DOI: 10.1152/jn.00410.2016

Visuomotor learning in one limb often confers benefits in performance with the other limb, a phenomenon known as interlimb transfer. In this study, we demonstrate for the first time that transfer of learning across limbs can be dissociated into explicit and implicit components and that the extent to which these distinct components of learning transfer to the opposite limb is constrained by the alignment of the learned compensation in joint-based and extrinsic coordinates.

Competition between movement plans increases motor variability: evidence of a shared resource for movement planning
Leonie Oostwoud Wijdenes, Richard B. Ivry, Paul M. Bays
September 1, 2016 : 1295-1303
DOI: 10.1152/jn.00113.2016

Various lines of evidence indicate that multiple movements can be prepared in parallel. Here, we show that preparing more than one movement comes with a cost: a movement plan is more variable if it is prepared simultaneously with another plan. This suggests that the representations of movement plans share a common neural resource and implies that the number of alternative plans is constrained by noise.

Motor unit activity in biceps brachii of left-handed humans during sustained contractions with two load types
Jeffrey R. Gould, Brice T. Cleland, Diba Mani, Ioannis G. Amiridis, Roger M. Enoka
September 1, 2016 : 1358-1365
DOI: 10.1152/jn.00147.2016

Adjustments in discharge characteristics of biceps brachii motor units during sustained submaximal contractions differ when the arm supports an inertial load (position control) compared with pulling against a rigid restraint (force control). The present study demonstrates that the adjustments occur more rapidly and to a greater extent during position control for left-handers, as has been reported previously for right-handers.

Velocity dependence of vestibular information for postural control on tilting surfaces
Fay B. Horak, JoAnn Kluzik, Frantisek Hlavacka
September 1, 2016 : 1468-1479
DOI: 10.1152/jn.00057.2016

The relative use of vestibular vs. somatosensory information for human balance control is unclear. When standing with eyes closed, subjects with vestibular loss were most unstable within a critical surface tilt velocity range of 2 to 8 deg/s. We propose that the vestibular system is critical for controlling balance at tilt velocities around normal postural sway, whereas graviceptive control is used at lower velocities, and proprioceptively triggered automatic postural responses are used at higher velocities.

Higher Neural Functions and Behavior

A two-stage model of concurrent interval timing in monkeys
Matthew R. Kleinman, Hansem Sohn, Daeyeol Lee
September 1, 2016 : 1068-1081
DOI: 10.1152/jn.00375.2016

How accurately animals can estimate the duration of elapsed time for multiple intervals simultaneously has not been investigated rigorously. In this study, we show that monkeys can time two concurrent intervals accurately with weakly dilated subjective time for the second overlapping interval.

Acute ethanol effects on neural encoding of reward size and delay in the nucleus accumbens
Andrea L. Gutman, Sharif A. Taha
September 1, 2016 : 1175-1188
We report ethanol effects on nucleus accumbens (NAcc) firing while rats respond for rewards differing in delay or size. First, ethanol administration caused a loss of value encoding in cue-responsive NAcc neurons in rats responding for immediate or delayed rewards. Second, ethanol selectively attenuated lever press-evoked firing on delayed reward trials. This was accompanied by increased latency to respond for delayed rewards. Our results suggest that ethanol effects on NAcc encoding may contribute to ethanol-induced impulsivity.

Feature-based attention and spatial selection in frontal eye fields during natural scene search
Pavan Ramkumar, Patrick N. Lawlor, Joshua I. Glaser, Daniel K. Wood, Adam N. Phillips, Mark A. Segraves, Konrad P. Kording
September 1, 2016 : 1328-1343

DOI: 10.1152/jn.01044.2015

Feature-based attention helps us to locate objects efficiently during visual search, but how the brain implements FBA in natural scenes remains an open question. We trained macaque monkeys to search for targets in natural scenes while recording from the frontal eye field (FEF). Although the monkeys performed the task well, we found that task-relevant visual features were weak predictors of gaze behavior. Furthermore, we found that task-relevant visual features did not modulate FEF activity.

Pain anticipatory phenomena in patients with central poststroke pain: a magnetoencephalography study
Raghavan Gopalakrishnan, Richard C. Burgess, Scott F. Lempka, John T. Gale, Darlene P. Floden, Andre G. Machado
September 1, 2016 : 1387-1395

DOI: 10.1152/jn.00215.2016

Central poststroke pain is characterized by hemianesthesia associated with severe unremitting chronic pain. To date, treatments have focused exclusively on modulation of sensory pathways with analgesia being the end point. Because the final pain experience stems from sensory as well as affective components, integrative approaches are needed to relieve patients from pain-related disability. Pain affect in this population is poorly understood, including anticipatory phenomena. We present neural correlates of pain anticipation studied using magnetoencephalography.

Understanding location- and feature-based processing along the human intraparietal sulcus
Katherine C. Bettencourt, Yaoda Xu
September 1, 2016 : 1488-1497

DOI: 10.1152/jn.00404.2016

The human IPS has been subdivided according to multiple different organizational schemes. Here, we determined the localization of two visual short-term memory (VSTM) intraparietal sulcus (IPS) regions with respect to IPS topographic regions and the role of different IPS regions in location- and feature-based processing. We show that understanding the multiplex nature of IPS in visual cognition may only be achieved by examining how regions identified by different tasks and methods may colocalize with each other.

Nervous System Pathophysiology

Morphine-induced synaptic plasticity in the VTA is reversed by HDAC inhibition
Michael E. Authement, Ludovic D. Langlois, Haifa Kassis, Shawn Gouty, Matthieu Dacher, Ryan D. Shepard, Brian M. Cox, Fereshteh S. Nugent
September 1, 2016 : 1093-1103

DOI: 10.1152/jn.00238.2016

Learning mechanisms in brain reward pathways are hijacked after experience with drugs of abuse, shaping drug-related memories that underlie compulsive drug-taking behavior. Ventral tegmental area (VTA) dopamine neuronal dysfunction is an initial step for the development of addiction. Drugs of abuse may silence genes in the VTA, while compounds called histone deacetylase (HDAC) inhibitors may oppose this. We demonstrate that acute morphine-induced synaptic plasticities in the VTA are reversible by an HDAC inhibitor.

Neural Circuits

Organization of cortico-cortical pathways supporting memory retrieval across subregions of the left ventrolateral prefrontal cortex
Jennifer Barredo, Timothy D. Verstynen, David Badre
September 1, 2016 : 920-937

DOI: 10.1152/jn.00157.2016

High-angular-resolution diffusion imaging, deterministic tractography, and functional connectivity were used to analyze the connectivity of the human ventrolateral prefrontal cortex (VLPFC). Evidence is provided for separate ventral and dorsal connectivity zones within VLPFC. Data suggest that dorsal VLPFC as a whole is part of a general cognitive control network, in contrast to earlier work suggesting that caudal VLPFC supports control cognitive whereas mid- to anterior VLPFC is functionally important for language and semantic processing.

A combined TMS-EEG study of short-latency afferent inhibition in the motor and dorsolateral prefrontal cortex
Yoshihiro Noda, Robin F. H. Cash, Reza Zomorrodi, Luis Garcia Dominguez, Faranak Farzan, Tarek K. Rajji, Mera S. Barr, Robert Chen, Zafiris J.
Short-latency afferent inhibition (SAI) is a transcranial magnetic stimulation (TMS) paradigm that has previously been shown to be a reliable measure of cholinergic activity in the motor cortex. In the present study, we extended the SAI paradigm to the dorsolateral prefrontal cortex (DLPFC) using combined TMS-EEG. We identified that the optimal interstimulus interval of SAI from the DLPFC is N20 + 4 ms and its spatiotemporal profile is characterized by the modulation of N100 at the left frontal cortex.

Two classes of excitatory synaptic responses in rat thalamic reticular neurons
Charlotte Deleuze, John R. Huguenard
September 1, 2016: 995-1011
DOI: 10.1152/jn.01121.2015

The thalamic reticular nucleus provides feedforward and feedback inhibition to thalamocortical relay neurons. A minimal stimulation approach was used to isolate and characterize the two main excitatory inputs from the cortex and thalamus to this nucleus. Thalamic inputs were larger and had faster \( \alpha \)-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor kinetics, promoting rapid feedback inhibition, whereas cortical inputs were kinetically slower and recruited a greater contribution from N-methyl-d-aspartate receptors, leading to more integrative feedback.

Functional evidence for a direct excitatory projection from the lateral habenula to the ventral tegmental area in the rat
P. Leon Brown, Paul D. Shepard
September 1, 2016: 1161-1174
DOI: 10.1152/jn.00305.2016

Changes in the phasic activity of midbrain dopamine neurons are associated with reward processing. The lateral habenula inhibits dopamine neurons indirectly, but there is also evidence for a direct, albeit weak, excitatory influence. Here, we confirm the existence of a habenular projection to midbrain dopamine neurons that is excitatory and more pronounced than previously thought. This input, which appears to be latent under normal conditions, may modulate dopamine neuron activity during exposure to aversive stimuli.

Stochastic slowly adapting ionic currents may provide a decorrelation mechanism for neural oscillators by causing wander in the intrinsic period
Sharon E. Norman, Robert J. Butera, Carmen C. Canavier
September 1, 2016: 1189-1198
DOI: 10.1152/jn.00193.2016

We study the firing statistics of spontaneously firing pacemaker neurons. The autocorrelation structure of the firing events reveal slow trends in the period as well as a tendency to minimize short-term fluctuations. A phenomenological model (autoregressive move average) and a biophysical model (integrate and fire) with stochastic and deterministic components capture the autocorrelation structure. We suggest that this structure is a neural signature of a stochastic, slowly adapting population of ion channels.

Spike synchrony generated by modulatory common input through NMDA-type synapses
Nobuhiko Wagatsuma, Rüdiger von der Heydt, Ernst Niebur
September 1, 2016: 1418-1433
DOI: 10.1152/jn.01142.2015

Recent neurophysiological results showing that in V1 and V2, presumed modulatory top-down input due to contour grouping increases synchrony but that additional modulatory input due to top-down attention does not change tight synchrony (correlations on the order of milliseconds) and decreases loose synchrony (tens of milliseconds). These findings are understood from our model of integrate-and-fire neurons under the assumption that contour grouping as well as attention lead to additive modulatory common input through N-methyl-d-aspartate-type synapses.

Decreased cerebellar-cerebral connectivity contributes to complex task performance
Curren Katz, André Knops
September 1, 2016: 1434-1448
DOI: 10.1152/jn.00684.2015

The cerebellum supports cognitive task performance through bidirectional task-driven connectivity with the cerebral cortex. Previous neuroimaging studies have found coactivation of cerebellar and cerebral regions when subjects performed relatively complex tasks. Here we show that cerebellar lobule VI connectivity with posterior parietal, cingulate, and frontal regions decreases with increasing task complexity. Thus increased cerebellar-cerebral connectivity in relatively simple, automated tasks and decreased connectivity in more demanding tasks may contribute to cognitive performance.

Sensory Processing
Relationship of membrane properties, spike burst responses, laminar location, and functional class of dorsal horn neurons recorded in vitro
Patrick M. Dougherty, Jinghong Chen
September 1, 2016 : 1137-1151
DOI: 10.1152/jn.00187.2016

This work shows that grouping spinal neurons by response to afferent input provides the strongest correlation to both passive and active membrane properties.

Looking for symmetry: fixational eye movements are biased by image mirror symmetry
Andrew Isaac Meso, Anna Montagnini, Jason Bell, Guillaume S. Masson
September 1, 2016 : 1250-1260
DOI: 10.1152/jn.01152.2015

This work presents the novel finding that small fixational eye movements made by humans viewing synthetic scenes have their directions strongly distorted in the presence of symmetry. The distortion results in a bias parallel to axes of symmetry measured across various task conditions and found to be persistent for up to 3 s. We argue that this automated process serves a functional role for active vision.

Target-specific M1 inputs to infragranular SI pyramidal neurons
Amanda K. Kinnischtzke, Erika E. Fanselow, Daniel J. Simons
September 1, 2016 : 1261-1274
DOI: 10.1152/jn.01032.2015

We examined the specificity of primary motor cortex (M1) inputs to specific classes of primary somatosensory cortex (SI) pyramidal neurons and found that M1 axons synapse on infragranular SI neurons with greater selectivity than previously appreciated. These results suggest M1 can differentially regulate particular circuits in SI under conditions of high M1 activity (e.g., whisking). Additionally, each type of pyramidal neuron has a unique set of intrinsic properties that allow them function differently within the circuit.

Perception of combined translation and rotation in the horizontal plane in humans
Benjamin T. Crane
September 1, 2016 : 1275-1285
DOI: 10.1152/jn.00322.2016

During human ambulation, rotation and translation occur simultaneously, such that lateral translation is coupled with inward rotation. However, there has been little previous work on how these combined movements are perceived. The current study determined the bias and threshold of human perception during such combined movements and found concurrent rotation biases perception of lateral translation, such that translation occurring during ambulation is likely to be perceived only as rotation.

Nonlinear computations shaping temporal processing of precortical vision
Daniel A. Butts, Yuwei Cui, Alexander R. R. Casti
September 1, 2016 : 1344-1357
DOI: 10.1152/jn.00878.2015

This work describes how nonlinear processing of the visual stimulus evolves across successive stages of neural processing: the retina and lateral geniculate nucleus (LGN), using paired recordings of LGN neurons and their primary retinal input. Nonlinear modeling is used to demonstrate that temporal patterning of LGN spikes is largely established in the retina and amplified in the LGN by temporal integration and thresholding. We also detected smaller inputs added at the level of the LGN.

Relating normalization to neuronal populations across cortical areas
Douglas A. Ruff, Joshua J. Alberts, Marlene R. Cohen
September 1, 2016 : 1375-1386
DOI: 10.1152/jn.00017.2016

Normalization is thought to underlie many sensory, motor, and cognitive processes and likely arises from interactions between neuronal populations. To gain insight into normalization mechanisms, we recorded the activity of populations of neurons in response to combinations of visual stimuli. We found that neurons that show strong normalization shared less trial-to-trial variability with other neurons in the same cortical area and more variability with neurons in other cortical areas than did units with weak normalization.

A simple approach to ignoring irrelevant variables by population decoding based on multisensory neurons
HyungGoo R. Kim, Xaq Pitkow, Dora E. Angelaki, Gregory C. DeAngelis
September 1, 2016 : 1449-1467
DOI: 10.1152/jn.00005.2016
Sensory signals often reflect multiple variables that change in the environment. To estimate one task-relevant variable and ignore others, the brain needs to perform marginalization, which involves computing the probability distribution over one variable while averaging over irrelevant variables. We describe a computational approach by which a linear transformation of neural population responses can approximate marginalization. We show, through simulations involving diverse multisensory neurons, that this approach is effective in dissociating self-motion from object motion.

**Vestibular and oculomotor influences on visual dependency**
R. Edward Roberts, Mariane Da Silva Melo, Aazim A. Siddiqui, Qadeer Arshad, Mitesh Patel
September 1, 2016 : 1480-1487
DOI: 10.1152/jn.00895.2015

Participants made verticality judgments using the rod-and-disk test, a test of visual dependence, and then repeated after caloric irrigation. If the combination of rotating disk and caloric increased the slow-phase velocity of the torsional nystagmus the tilt in subjective verticality increased, whereas reductions in eye velocity were associated with reduced tilt. Thus visual dependency measures are not only modulated by perceptual style but can also reflect local vestibulo-ocular function, specifically torsional eye movements.

**Oculomotor inhibition covaries with conscious detection**
Alex L. White, Martin Rolfs
September 1, 2016 : 1507-1521
DOI: 10.1152/jn.00268.2016

The eyes freeze in response to stimulus onsets. We developed a novel method to compare the sensitivity of this involuntary reflex to that of explicit perceptual detection. The two responses had similar contrast thresholds and were similarly affected by pattern adaptation. They also covaried across individual trials: the eyes froze if and only if the observer reported seeing a stimulus, even when none was present. Oculomotor inhibition therefore rapidly reveals the state of conscious perception.

**Optimal visuotactile integration for velocity discrimination of self-hand movements**
M. Chancel, C. Blanchard, M. Guerraz, A. Montagnini, A. Kavounoudias
September 1, 2016 : 1522-1535
DOI: 10.1152/jn.00883.2015

The present study demonstrates, for the first time, that kinesthetic information of visual and tactile origins are optimally integrated (Bayesian modeling) to improve velocity discrimination for self-hand movement. We used an original paradigm consisting of similar illusory hand movements induced through visual and tactile stimulation. By testing the role of other sources of information favoring nonmoving hand perception, we also highlight the key contribution of the omnipresent muscle proprioceptive information and its overweighting for kinesthesia.

**Rapid Report**

**Human parietal cortex lesions impact the precision of spatial working memory**
Wayne E. Mackey, Orrin Devinsky, Werner K. Doyle, John G. Golfinos, Clayton E. Curtis
September 1, 2016 : 1049-1054
DOI: 10.1152/jn.00380.2016

Working memory (WM) is a critical building block for nearly all high-level cognitive functions. Although it is widely acknowledged that WM involves distributed processing throughout the brain, precisely which brain areas are critical for supporting WM remains unknown. In this study, we find that lesions to human posterior parietal cortex (PPC) impair the precision of spatial WM, but not visuomotor control. Therefore, human PPC is essential for spatial WM.

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**Inadequate reporting of statistical results**
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Original Research

Contraction mode itself does not determine the level of mTORC1 activity in rat skeletal muscle
Satoru Ato, Yuhei Makanae, Kohei Kido, Satoshi Fujita
September 28, 2016 : e12976

DOI: 10.14814/phy2.12976

It is well known that divergence of contraction mode in resistance exercise modulates mTORC1 activity differently, although mechanisms were still unknown. In this study, we found that divergence of contraction mode itself does not determine level of mTORC1 activity, but differences in the force-time integral during muscle contraction determines mTORC1 activity in rat skeletal muscle.

W’ expenditure and reconstitution during severe intensity constant power exercise: mechanistic insight into the determinants of W'
Ryan M. Broxterman, Phillip F. Skiba, Jesse C. Craig, Samuel L. Wilcox, Carl J. Ade, Thomas J. Barstow
September 28, 2016 : e12856

DOI: 10.14814/phy2.12856

In conclusion, the W’BAL model is able to characterize the expenditure and reconstitution of W’ across the contraction–relaxation cycles of severe intensity constant power handgrip exercise. Moreover, the reconstitution of W’ during constant power exercise is influenced by the power output within the severe intensity domain, the duration of relaxation between contractions, and CP.

Leucine-rich repeat containing protein LRRC8A is essential for swelling-activated Cl− currents and embryonic development in zebrafish
Toshiki Yamada, Robert Wondergem, Rebecca Morrison, Viravuth P. Yin, Kevin Strange
September 28, 2016 : e12940

DOI: 10.14814/phy2.12940

A volume-regulated anion channel (VRAC) has been electrophysiologically characterized in innumerable mammalian cell types. Recent studies have identified the mammalian leucine-rich repeat containing protein LRRC8A as an essential VRAC component. Our studies provide confirmation of the importance of LRRC8A in VRAC activity and establish the zebrafish as a model system for characterizing the molecular regulation and physiological roles of VRAC and LRRC8 proteins.

Plasma acylcarnitine profiling indicates increased fatty acid oxidation relative to tricarboxylic acid cycle capacity in young, healthy low birth weight men
Amalie Ribel-Madsen, Rasmus Ribel-Madsen, Charlotte Brøns, Christopher B. Newgard, Allan A. Vaag, Lars I. Hellgren

September 28, 2016 : e12795

DOI: 10.14814/phy2.12795

A number of studies have demonstrated that fatty acid oxidation and ketogenesis are increased in young, healthy low birth weight men. The aim of this study was to determine whether plasma acylcarnitines are indicative of increased fatty acid oxidation when compared to tricarboxylic acid cycle capacity.
Low birth weight (LBW) men had higher fasting plasma levels of several acylcarnitine species compared with normal birth weight (NBW) men, including higher C2 and C4-OH levels, indicating an increased fatty acid beta-oxidation relative to the tricarboxylic acid cycle flux, and higher C6-DC, C10-OH/C8-DC, and total hydroxyl-/dicarboxyl-acylcarnitine levels, suggesting an increased fatty acid omega-oxidation. Total hydroxyl-/dicarboxyl-acylcarnitine level tended to be negatively associated with the hepatic insulin resistance index, suggesting that omega-oxidation could be a scavenger pathway to prevent an accumulation of lipid species that impair insulin signaling in the liver.

**Reduced mitochondrial mass and function add to age-related susceptibility toward diet-induced fatty liver in C57BL/6J mice**
Kerstin Lohr, Fiona Pachl, Amin Moghaddas Gholami, Kerstin E. Geillinger, Hannelore Daniel, Bernhard Kuster, Martin Klingenspor
September 29, 2016 : e12988
DOI: 10.14814/phy2.12988

Our study elucidated the early changes in liver physiology upon feeding a high fat diet investigated in three age groups of C57BL/6J mice. Intriguingly, the interaction between high fat diet and increasing age enforces the accumulation of fat in the liver while reducing mitochondrial mass and function.

**AT-RvD1 combined with DEX is highly effective in treating TNF-α-mediated disruption of the salivary gland epithelium**
Justin T. Easley, Christina L. M. Maruyama, Ching-Shuen Wang, Olga J. Baker
September 29, 2016 : e12990
DOI: 10.14814/phy2.12990

Par-C10 cells form three-dimensional structures when grown on Matrigel. The proinflammatory cytokine TNF-alpha causes disruption of cell cluster formation. However, treatment with resolvin D1 and dexamethasone ameliorates this effect.

**Videomicroscopy as a tool for investigation of the microcirculation in the newborn**
Ian M. R. Wright, Joanna L. Latter, Rebecca M. Dyson, Chris R. Levi, Vicki L. Clifton
September 29, 2016 : e12941
DOI: 10.14814/phy2.12941

This paper delineates the normal values obtained for a whole series of videomicroscopic structural and functional parameters in the newborn over the first 3 days of life. This lays the groundwork for future videomicroscopic assessment of the cutaneous microcirculation in the sicker and more premature infant, as well as for future studies of programmed changes in microcirculatory physiology.

**Motor unit number estimates and neuromuscular transmission in the tibialis anterior of master athletes: evidence that athletic older people are not spared from age-related motor unit remodeling**
Mathew Piasecki, Alex Ireland, Jessica Coulson, Dan W. Stashuk, Andrew Hamilton-Wright, Agnieszka Swiecicka, Martin K. Rutter, Jamie S. McPhee, David A. Jones
September 30, 2016 : e12987
DOI: 10.14814/phy2.12987

MRI images of the lower leg of Young, Old, and Master Athlete participants.

**The vestibular system is critical for the changes in muscle and bone induced by hypergravity in mice**
Naoyuki Kawao, Hironobu Morita, Koji Obata, Yukinori Tamura, Katsumi Okumoto, Hiroshi Kaji
October 2, 2016 : e12979
DOI: 10.14814/phy2.12979

We investigated the role of vestibular signaling and sympathetic outflow in the effects of hypergravity on muscle and bone using vestibular-lesioned mice and propranolol, a blocker of β-adrenergic receptors. We found that gravity changes affect muscle and bone through vestibular signals and subsequent sympathetic outflow in mice.

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Exposure of C57BL/6J mice to long photoperiod during early life stages increases body weight and alters plasma metabolomic profiles in adulthood
Tatsuhiro Uchiwa, Yusuke Takai, Ayako Tashiro, Mitsuhiro Furuse, Shinobu Yasuo
September 19, 2016 : e12974
DOI: 10.14814/phy2.12974

Postnatal exposure of C57BL/6J mice to long photoperiod induces increase in body weight until adulthood. Various changes in plasma metabolic profiles during adulthood were observed in the mice exposed to long photoperiod postnatally.

Understanding the link between somatosensory temporal discrimination and movement execution in healthy subjects
Antonella Conte, Daniele Belvisi, Nicoletta Manzo, Matteo Bologna, Francesca Barone, Matteo Tartaglia, Neeraj Upadhyay, Alfredo Berardelli
September 19, 2016 : e12899
DOI: 10.14814/phy2.12899

The human brain relies fundamentally on interdependent sensory and motor networks. Sensory-motor interplay depends essentially on temporal sensory information processing.

Temporal sensory processing is impaired in patients with basal ganglia disorders (Parkinson's disease and dystonia).

Precisely what these altered somatosensory temporal discrimination threshold (STDT) values imply in movement disorders remains unclear.

In healthy subjects movement execution gates STDT processing at movement onset and up to 200 msec thereafter possibly through subcortical sensory gating mechanisms.

Effects of high EPA and high DHA fish oils on changes in signaling associated with protein metabolism induced by hindlimb suspension in rats
Gabriel Nasri Marzuca-Nasr, Kaio Fernando Vitzel, Luis Gustavo De Sousa, Gilson M. Murata, Amanda Rabello Crisma, Carlos Flores Rodrigues Junior, Phablo Abreu, Rosângela Pavan Torres, Jorge Mancini-Filho, Sandro M. Hirabara, Philip Newsholme, Rui Curi
September 19, 2016 : e12958
DOI: 10.14814/phy2.12958

The treatment with effects of either eicosapentaenoic (EPA)-rich or docosahexaenoic (DHA)-rich fish oil increased omega-3 fatty acid and changed protein synthesis signaling in skeletal muscle under conditions of atrophy. The effects of EPA-rich fish oil on protein synthesis signaling were more pronounced and so this fish oil type might be further investigated in conditions of less intense skeletal muscle mass loss.

Microstructural characterization of myocardial infarction with optical coherence tractography and two-photon microscopy
Craig J. Goergen, Howard H. Chen, Sava Sakadžić, Vivek J. Srinivasan, David E. Sosnovik
September 19, 2016 : e12894
DOI: 10.14814/phy2.12894

Nondestructive optical imaging approaches can be used to characterize myocardial microstructure in infarcted mouse hearts. Optical coherence tractography revealed the loss of tract coherence and decreased penetration depth within the infarct zone. Segmented two-photon microscopy images revealed increased collagen in the infarct, potentially explaining the increased light attenuation, and furthermore, that collagen fibers in the infarct display structural coherence only when adjacent to residual myofibers. Thus, myocardial microstructure after infarctions is a heterogeneous mix of both organized and highly disorganized regions.

Cycle training modulates satellite cell and transcriptional responses to a bout of resistance exercise
Kevin A. Murach, R. Grace Walton, Christopher S. Fry, Sami L. Michaelis, Jason S. Groshong, Brian S. Finlin, Philip A. Kern, Charlotte A. Peterson
September 19, 2016 : e12973
DOI: 10.14814/phy2.12973

This investigation evaluated whether moderate-intensity cycle ergometer training affects satellite cell and molecular responses to acute maximal concentric/eccentric resistance exercise in middle-aged women. Moderate-intensity endurance cycle training modulates the response to acute resistance exercise, potentially conditioning the muscle for more intense concentric/eccentric activity. Furthermore, cycle training is an effective endurance exercise modality for promoting growth, specifically in middle-aged women who are susceptible to muscle mass loss with progressing age.

The differential effects of azithromycin on the airway epithelium in vitro and in vivo
Azithromycin (AZM) has been shown to improve clinical outcomes in several respiratory diseases, however, the mechanisms remain to be resolved. We demonstrate that AZM enhanced barrier integrity, increased thickness, suppressed mucin production, and MMP-9 release during the formation of a normal epithelial barrier in vitro.

To complement in vitro studies, we recruited 10 patients with moderate-severe asthma and investigated airway epithelial changes (via bronchoscopy) pre- and post-AZM treatment, but did not identify evidence of increased epithelial barrier thickness or decreased mucin production.

Thyroid hormone treatment decreases hepatic glucose production and renal reabsorption of glucose in alloxan-induced diabetic Wistar rats
September 21, 2016 : e12961
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T3 reduces blood glucose and hepatic glucose production, as well as PEPCK, GAPDH and pAKT content in the liver and decreases renal expression of SGLT2, renal glucose uptake, and increased glucosuria. The results suggest that the decreased hepatic glucose output and increased glucose excretion induced by T3 treatment are important mechanisms that contribute to reduce the serum concentration of glucose, accounting for the improvement of glucose homeostasis control in diabetic rats.

Neurons in primary visual cortex represent distribution of luminance
Yong Wang, Yi Wang
September 21, 2016 : e12966
DOI: 10.14814/phy2.12966

Luminance is the most fundamental visual attribute and is important for object perception. The authors demonstrate that neurons in the primary visual cortex not only code luminance change, but also change of luminance distribution, suggesting the neural mechanism for sensing luminance change when the global distribution of luminance varies.

CC-chemokine receptor 7 (CCR7) deficiency alters adipose tissue leukocyte populations in mice
Jeb S. Orr, Arion J. Kennedy, Andrea A. Hill, Emily K. Anderson-Baucum, Merla J. Hubler, Alyssa H. Hasty
September 21, 2016 : e12971
DOI: 10.14814/phy2.12971

We sought to determine the impact of CCR7 on adipose tissue (AT) immune cell content in lean and obese mice. Although there were no changes in AT macrophages, CD8 T cells preferentially accumulated in the AT of CCR7-/− mice.

Gender differences in HR kinetics at the onset of moderate and heavy exercise intensity in adolescents
Nicola Lai, Alessandro Martis, Alfredo Belfiori, Fatima Tolentino-Silva, Melita M. Nasca, James Strainic, Marco E. Cabrera
September 21, 2016 : e12970
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The and heart rate (HR) dynamic responses to square-wave exercise of moderate and heavy intensity were analyzed in a group of female and male adolescents. Gender differences in theand HR kinetics suggest that oxygen delivery and utilization kinetics of female adolescents differ from those in male adolescents. The faster HR kinetics in male than female and the association between HR and kinetics in male can in part explain the gender differences observed in kinetics.

Sex differences in adult rat insulin and glucose responses to arginine: programming effects of neonatal separation, hypoxia, and hypothermia
Ashley L. Gehrand, Brian Hoeynck, Mack Jablonski, Cole Leonovicz, Risheng Ye, Phillipp E. Scherer, Hershel Raff
September 22, 2016 : e12972
DOI: 10.14814/phy2.12972

This study evaluated the programming effects in adult male and female rats of maternal separation of neonatal rats exposed to normoxia (control), hypoxia allowing spontaneous hypothermia, hypothermia per se, or hypoxia while maintaining isothermia with external heat. The magnitude of the insulin response to arginine was much greater in adult males compared to females and was augmented in adult males exposed to maternal separation as neonates.
Exercise training increases protein O-GlcNAcylation in rat skeletal muscle
Kristin Halvorsen Hortemo, Per Kristian Lunde, Jan Haug Anonsen, Heidi Kvaløy, Morten Munkvik, Tommy Aune Rehn, Ivar Sjaastad, Ida Gjervold Lunde, Jan Magnus Aronsen, Ole M. Sejersted
September 22, 2016 : e12896
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Long-term exercise training by treadmill running increased protein O-GlcNAcylation in rat skeletal muscle. There was a striking increase in O-GlcNAcylation of cytoplasmic proteins ~50 kDa in size that judged from mass spectrometry could represent O-GlcNAcylation of one or more key metabolic enzymes. This suggests that O-GlcNAcylation of cytoplasmic proteins is part of the training response in skeletal muscle. Furthermore, human skeletal muscle displayed extensive protein O-GlcNAcylation that by large mirrored the fiber-type-related pattern in rats, suggesting O-GlcNAcylation as an important signaling system also in human muscle.

Plasminogen activator inhibitor-1 does not contribute to the pulmonary pathology induced by acute exposure to ozone
September 25, 2016 : e12983
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This study investigates the contribution of plasminogen activator inhibitor (PAI)-1 to the pulmonary pathology induced by acute exposure to ozone in mice. Although acute exposure to ozone increases PAI-1 in the lung, PAI-1 does not functionally contribute to any aspect of the pulmonary pathology induced by acute exposure to ozone.

The role of atrial natriuretic peptide to attenuate inflammation in a mouse skin wound and individually perfused rat mesenteric microvessels
Fitz-Roy E. Curry, Joyce F. Clark, Yanyan Jiang, Min-Ho Kim, Roger H. Adamson, Scott I. Simon
September 25, 2016 : e12968
DOI: 10.14814/phy2.12968

We have shown that atrial natriuretic peptide (ANP) attenuates leukocyte–endothelial interactions in cultured endothelial cells. Here, we evaluate for the first time the contribution of this mechanism to attenuate inflammatory mechanisms in intact microvessels. These observations provide the basis for further basic and clinical investigations of ANP as vasoprotective agent.

Unexpected effects of the MIP-CreER transgene and tamoxifen on β-cell growth in C57Bl6/J male mice
Bethany A. Carboneau, Thao D. V. Le, Jennifer C. Dunn, Maureen Gannon
September 25, 2016 : e12863
DOI: 10.14814/phy2.12863

Carboneau et al. demonstrate that the MIP-CreER transgene, which contains the human growth hormone mini gene, affects beta cell mass via increased individual beta cell size rather than increased beta cell proliferation. In addition, they show that tamoxifen can impair high fat diet-induced β-cell proliferation in the absence of any additional genetic manipulation.

Serum lipase activity and concentration during intravenous infusions of GLP-1 and PYY3-36 and after ad libitum meal ingestion in overweight men
Julie B. Schmidt, Anders Sjödin, Lene S. Stevner, Christian Ritz, Natasha B. Michaelsen, Anne B. Thomsen, Jens J. Holst, Arne Astrup
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Previously, we investigated the effect of intravenous infusion of GLP-1 and PYY3-36 separately and in combination, on energy intake, energy expenditure, and appetite sensations in healthy overweight men. Here, we report additional data to elucidate whether infusion of GLP-1 and PYY3-36 as well as an ad libitum meal increases serum lipase.

Associations between measures of vascular structure and function and systemic circulating blood markers in humans
Lisa M. Cotie, Katharine D. Currie, Greg M. McGill, Austin J. Cameron, Alison S. McFadden, Stuart M. Phillips, Maureen J. MacDonald
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Across a range of vascular health, moderate relationships were observed between markers of type I collagen turnover and functional measures of arterial stiffness and between a marker of vasoconstriction and a measure of endothelial function. These results indicate that, while there may be
regulatory links between the indices examined, monitoring systemic blood markers rather than functional vascular measures may not be sufficient to assess vascular structure and function.

Hyperosmolality regulates UT-A6 urea transporter expression in the Caco-2 cell line
Alison McGrane, Gavin Stewart
September 25, 2016 : e12984
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UT-A6 urea transporters are located in the human colon, but little is known regarding their regulation. Using the Caco-2 cell line and quantitative PCR, this study has shown that hyperosmolality significantly upregulates UT-A6 expression. Furthermore, it appears that the regulatory pathway concerned with this effect is similar to that reported previously for renal UT-A transporters and involves a calcium-dependent protein kinase C protein.

Inhibition of alveolar Na transport and LPS causes hypoxemia and pulmonary arterial vasoconstriction in ventilated rats
Bodo Davieds, Julian Gross, Marc M. Berger, Emel Baloğlu, Peter Bärtsch, Heimo Mairbäurl
September 25, 2016 : e12985
DOI: 10.14814/phy2.12985

Inhibition of lung fluid reabsorption by inhibition of Na transport in alveolar epithelium with amiloride and lipopolisaccharide impairs oxygen diffusion, likely by alveolar edema. This results in hypoxemia, and causes a similar degree of increase in pulmonary arterial pressure as ventilating rats with hypoxic gas.
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