

IN THIS ISSUE

- 2287** In This Issue of *Diabetes*

PERSPECTIVES IN DIABETES

- 2289** Cellular Senescence in Type 2 Diabetes: A Therapeutic Opportunity
A.K. Palmer, T. Tchkonia, N.K. LeBrasseur, E.N. Chini, M. Xu, and J.L. Kirkland
- 2299** Biologic Responses to Weight Loss and Weight Regain: Report From an American Diabetes Association Research Symposium
R.L. Leibel, R.J. Seeley, T. Darsow, E.G. Berg, S.R. Smith, and R. Ratner
- 2310** Gut Peptides Are Novel Regulators of Intestinal Lipoprotein Secretion: Experimental and Pharmacological Manipulation of Lipoprotein Metabolism
C. Xiao, S. Dash, C. Morgantini, K. Adeli, and G.F. Lewis

COMMENTARIES

- 2319** GLP-1R Agonists and Endothelial Dysfunction: More Than Just Glucose Lowering?
J. Lovshin and D. Cherney
- 2322** Hypoglycemia-Associated Autonomic Failure in Diabetes: Maladaptive, Adaptive, or Both?
P.E. Cryer
- 2324** Defective Glucagon-Like Peptide 1 Secretion in Prediabetes and Type 2 Diabetes Is Influenced by Weight and Sex. Chicken, Egg, or None of the Above?
A. Vella and C. Cobelli
- 2326** Interaction of Adipogenesis and Angiogenesis in Dietary-Induced Obesity
G. Jia, L.A. Martinez-Lemus, and J.R. Sowers
- 2329** An Innate Disposition for a Healthier Gut: GLP-1R Signaling in Intestinal Epithelial Lymphocytes
W. Rosario and D. D'Alessio
- 2332** PET Measurements of Organ Metabolism: The Devil Is in the Details
K.I. Shoghi and R.J. Gropler
- 2335** Evidence for Residual and Partly Repairable Insulin Secretory Function and Maintained β -Cell Gene Expression in Islets From Patients With Type 1 Diabetes
L.S. Satin and S. Schnell

- 2338** Intestinal Lipoprotein Secretion: Incretin-Based Physiology and Pharmacology Beyond Glucose
R.H. Eckel

- 2341** New Piece in the Jigsaw Puzzle: Adipose Tissue-Derived Stem Cells From Obese Subjects Drive Th17 Polarization
B. Csóka, P. Pacher, P. Bai, and G. Haskó
- 2344** Blood Lipids and Type 2 Diabetes Risk: Can Genetics Help Untangle the Web?
D.I. Swerdlow and N. Sattar

DIABETES SYMPOSIUM: BROWNING OF ADIPOSE TISSUE—WHAT'S NEW?

This section features four articles from the 2nd *Diabetes* Symposium, held in conjunction with the ADA's 75th Scientific Sessions in Boston, MA, 5–9 June 2015.

- 2346** Brown and Beige Fat: Molecular Parts of a Thermogenic Machine
P. Cohen and B.M. Spiegelman
- 2352** Human Brown Adipose Tissue: What We Have Learned So Far
M.J. Betz and S. Enerbäck
- 2361** Exercise Effects on White Adipose Tissue: Beiging and Metabolic Adaptations
K.I. Stanford, R.J.W. Middelbeek, and L.J. Goodyear
- 2369** Transcriptional Regulatory Circuits Controlling Brown Fat Development and Activation
P. Seale

METABOLISM

- 2376** Evidence That in Uncontrolled Diabetes, Hyperglucagonemia Is Required for Ketosis but Not for Increased Hepatic Glucose Production or Hyperglycemia
T.H. Meek, M.D. Dorfman, M.E. Matsen, J.D. Fischer, A. Cubelo, M.R. Kumar, G.J. Taborsky Jr., and G.J. Morton
- 2388** Selective Impairment of Glucose but Not Fatty Acid or Oxidative Metabolism in Brown Adipose Tissue of Subjects With Type 2 Diabetes
D.P. Blondin, S.M. Labbé, C. Noll, M. Kunach, S. Phoenix, B. Guérin, É.E. Turcotte, F. Haman, D. Richard, and A.C. Carpenter
- 2398** Short-Chain Fatty Acids Protect Against High-Fat Diet-Induced Obesity via a PPAR γ -Dependent Switch From Lipogenesis to Fat Oxidation
G. den Besten, A. Bleeker, A. Gerding, K. van Eunen, R. Havinga, T.H. van Dijk, M.H. Oosterveer, J.W. Jonker, A.K. Groen, D.-J. Reijngoud, and B.M. Bakker

Keep up with the latest information for *Diabetes* and other ADA titles via Facebook (/ADAJournals) and Twitter (@ADA_Journals).

All articles in *Diabetes* are available online at diabetes.org/diabetes, are available free to print subscribers, or can be purchased as e-prints or reprints.

ADA's Diabetes Core Update podcast is available at diabetesjournals.org and through iTunes.

Icons shown below appear on the first page of an article if more information is available online.



Free Article



Video



Podcast



Supplementary Data



Companion Article

- 2409** GLP-1(32-36)amide Pentapeptide Increases Basal Energy Expenditure and Inhibits Weight Gain in Obese Mice
E. Tomas, V. Stanojevic, K. McManus, A. Khatri, P. Everill, W.W. Bachovchin, and J.F. Habener
- 2420** SUMO-Specific Protease 2 (SENP2) Is an Important Regulator of Fatty Acid Metabolism in Skeletal Muscle
Y.D. Koo, J.W. Choi, M. Kim, S. Chae, B.Y. Ahn, M. Kim, B.C. Oh, D. Hwang, J.H. Seol, Y.-B. Kim, Y.J. Park, S.S. Chung, and K.S. Park
- 2432** Effect of Sex and Impaired Glucose Tolerance on Organ-Specific Dietary Fatty Acid Metabolism in Humans
M. Kunach, C. Noll, S. Phoemix, B. Guérin, J.-P. Baillargeon, E.E. Turcotte, and A.C. Carpentier

OBESITY STUDIES

- 2442** Endostatin Prevents Dietary-Induced Obesity by Inhibiting Adipogenesis and Angiogenesis
H. Wang, Y. Chen, X.-a. Lu, G. Liu, Y. Fu, and Y. Luo
- 2457** Insulin Detemir Is Transported From Blood to Cerebrospinal Fluid and Has Prolonged Central Anorectic Action Relative to NPH Insulin
D.P. Begg, A.A. May, J.D. Mul, M. Liu, D.A. D'Alessio, R.J. Seeley, and S.C. Woods
- 2467** Dietary Intake, *FTO* Genetic Variants, and Adiposity: A Combined Analysis of Over 16,000 Children and Adolescents
Q. Qi, M.K. Downer, T.O. Kilpeläinen, H.R. Taal, S.J. Barton, I. Ntalla, M. Standl, V. Boraska, V. Huikari, J.C. Kieft-de Jong, A. Körner, T.A. Lakka, G. Liu, J. Magnusson, M. Okuda, O. Raitakari, R. Richmond, R.A. Scott, M.E.S. Bailey, K. Scheuermann, J.W. Holloway, H. Inskip, C.R. Isasi, Y. Mossavar-Rahmani, V.W.V. Jaddoe, J. Laitinen, V. Lindi, E. Melén, Y. Pitsiladis, N. Pitkänen, H. Snieder, J. Heinrich, N.J. Timpong, T. Wang, H. Yuji, E. Zeggini, G.V. Dedoussis, R.C. Kaplan, J. Wylie-Rosett, R.J.F. Loos, F.B. Hu, and L. Qi
- 2477** Adipose Tissue-Derived Stem Cells From Obese Subjects Contribute to Inflammation and Reduced Insulin Response in Adipocytes Through Differential Regulation of the Th1/Th17 Balance and Monocyte Activation
A. Eljaafari, M. Robert, M. Chehimi, S. Chanon, C. Durand, G. Vial, N. Bendridi, A.-M. Madec, E. Disse, M. Laville, J. Rieusset, E. Lefai, H. Vidal, and L. Pirola

ISLET STUDIES

- 2489** Inactivation of Protein Tyrosine Phosphatases Enhances Interferon Signaling in Pancreatic Islets
W.J. Stanley, S.A. Litwak, H.S. Quah, S.M. Tan, T.W.H. Kay, T. Tiganis, J.B. de Haan, H.E. Thomas, and E.N. Gurzov
- 2497** The Basic Helix-Loop-Helix Transcription Factor NEUROG3 Is Required for Development of the Human Endocrine Pancreas
P.S. McGrath, C.L. Watson, C. Ingram, M.A. Helmrath, and J.M. Wells
- 2506** Function of Isolated Pancreatic Islets From Patients at Onset of Type 1 Diabetes: Insulin Secretion Can Be Restored After Some Days in a Nondiabetogenic Environment In Vitro. Results From the DiViD Study
L. Krogvold, O. Skog, G. Sundström, B. Edwin, T. Buanes, K.F. Hanssen, J. Ludvigsson, M. Grabherr, O. Korsgren, and K. Dahl-Jørgensen

PATHOPHYSIOLOGY

- 2513** GLP-1 Response to Oral Glucose Is Reduced in Prediabetes, Screen-Detected Type 2 Diabetes, and Obesity and Influenced by Sex: The ADDITION-PRO Study
K. Færch, S.S. Torekov, D. Vistisen, N.B. Johansen, D.R. Witte, A. Jonsson, O. Pedersen, T. Hansen, T. Lauritzen, A. Sandbæk, J.J. Holst, and M.E. Jørgensen
- 2526** Cellular Stress, Excessive Apoptosis, and the Effect of Metformin in a Mouse Model of Type 2 Diabetic Embryopathy
Y. Wu, F. Wang, M. Fu, C. Wang, M.J. Quon, and P. Yang
- 2537** GLP-1R Agonists Modulate Enteric Immune Responses Through the Intestinal Intraepithelial Lymphocyte GLP-1R
B. Yusta, L.L. Baggio, J. Koehler, D. Holland, X. Cao, L.J. Pinnell, K.C. Johnson-Henry, W. Yeung, M.G. Surette, K.W.A. Bang, P.M. Sherman, and D.J. Drucker
- 2550** Adaptation of β -Cell and Endothelial Function to Carbohydrate Loading: Influence of Insulin Resistance
B.E. Hurwitz, N. Schneiderman, J.B. Marks, A.J. Mendez, A. Gonzalez, M.M. Llabre, S.R. Smith, R. Bizzotto, E. Santini, M.L. Manca, J.S. Skyler, A. Mari, and E. Ferrannini

COMPLICATIONS

- 2560** Neural Retinal Disorganization as a Robust Marker of Visual Acuity in Current and Resolved Diabetic Macular Edema
J.K. Sun, S.H. Radwan, A.Z. Soliman, J. Lammer, M.M. Lin, S.G. Prager, P.S. Silva, L.B. Aiello, and L.P. Aiello
- 2571** Effects of Acute and Antecedent Hypoglycemia on Endothelial Function and Markers of Atherothrombotic Balance in Healthy Humans
N.G. Joy, D.B. Tate, L.M. Younk, and S.N. Davis
- 2581** Therapeutic Potential of Anti-Angiogenic Multitarget *N,O*-Sulfated *E. Coli* K5 Polysaccharide in Diabetic Retinopathy
S. Rezzola, M. Dal Monte, M. Belleri, A. Bugatti, P. Chiodelli, M. Corsini, M. Cammalleri, A. Cancarini, L. Morbidelli, P. Oreste, P. Bagnoli, F. Semeraro, and M. Presta
- 2593** Inhibition of PAI-1 Via PAI-039 Improves Dermal Wound Closure in Diabetes
I.A. Rebalka, M.J. Raleigh, D.M. D'Souza, S.K. Coleman, A.N. Rebalka, and T.J. Hawke
- 2603** Hyperhexosemia-Induced Retinal Vascular Pathology in a Novel Primate Model of Diabetic Retinopathy
A. Chronopoulos, S. Roy, E. Beglova, K. Mansfield, L. Wachtman, and S. Roy

PHARMACOLOGY AND THERAPEUTICS

- 2609** Pathophysiological Mechanism of Bone Loss in Type 2 Diabetes Involves Inverse Regulation of Osteoblast Function by PGC-1 α and Skeletal Muscle Atrogenes: AdipoR1 as a Potential Target for Reversing Diabetes-Induced Osteopenia
M.P. Khan, A.K. Singh, A.A. Joharapurkar, M. Yadav, S. Shree, H. Kumar, A. Gurjar, J.S. Mishra, M.C. Tiwari, G.K. Nagar, S. Kumar, R. Ramachandran, A. Sharan, M.R. Jain, A.K. Trivedi, R. Maurya, M.M. Godbole, J.R. Gayen, S. Sanyal, and N. Chattopadhyay

- 2624** Exenatide Protects Against Glucose- and Lipid-Induced Endothelial Dysfunction: Evidence for Direct Vasodilation Effect of GLP-1 Receptor Agonists in Humans
J. Koska, M. Sands, C. Burciu, K.M. D'Souza, K. Raravikar, J. Liu, S. Truran, D.A. Franco, E.A. Schwartz, D.C. Schwenke, D. D'Alessio, R.Q. Migrino, and P.D. Reaven

- 2636** Adenylyl Cyclase Type 5 Deficiency Protects Against Diet-Induced Obesity and Insulin Resistance
D. Ho, X. Zhao, L. Yan, C. Yuan, H. Zong, D.E. Vatner, J.E. Pessin, and S.F. Vatner

GENETICS/GENOMES/PROTEOMICS/METABOLOMICS

- 2646** Role of Established Type 2 Diabetes–Susceptibility Genetic Variants in a High Prevalence American Indian Population
R.L. Hanson, R. Rong, S. Kobes, Y.L. Muller, E.J. Weil, J.M. Curtis, R.G. Nelson, and L.J. Baier

- 2658** Genetic Variant at the *GLUL* Locus Predicts All-Cause Mortality in Patients With Type 2 Diabetes
S. Prudente, H. Shah, D. Bailetti, M. Pezzolesi, P. Buranasupkajorn, L. Mercuri, C. Mendonca, S. De Cosmo, M. Niewczas, V. Trischitta, and A. Doria

- 2664** Epigenetic Regulation of Placenta-Specific 8 Contributes to Altered Function of Endothelial Colony-Forming Cells Exposed to Intrauterine Gestational Diabetes Mellitus
E.K. Blue, B.M. Sheehan, Z.V. Nuss, F.A. Boyle, C.M. Hocutt, C.R. Gohn, K.M. Varberg, J.N. McClintick, and L.S. Haneline

- 2676** Using Genetic Variants to Assess the Relationship Between Circulating Lipids and Type 2 Diabetes
T. Fall, W. Xie, W. Poon, H. Yaghootkar, R. Mägi, the GENESIS Consortium, J.W. Knowles, V. Lyssenko, M. Weedon, T.M. Frayling, and E. Ingelsson

ERRATUM

- 2685** Erratum. PD-L1–Driven Tolerance Protects Neurogenin3-Induced Islet Neogenesis to Reverse Established Type 1 Diabetes in NOD Mice. *Diabetes* 2015;64:529–540
R. Li, J. Lee, M.-s. Kim, V. Liu, M. Moulik, H. Li, Q. Yi, A. Xie, W. Chen, L. Yang, Y. Li, T.H. Tsai, K. Oka, L. Chan, and V. Yechoor

ISSUES AND EVENTS

- 2686** Issues and Events

e-LETTERS – COMMENTS AND RESPONSES

- e17** Comment on Vandal et al. Insulin Reverses the High-Fat Diet–Induced Increase in Brain A β and Improves Memory in an Animal Model of Alzheimer Disease. *Diabetes* 2014;63:4291–4301
H. Ghanim and P. Dandona

- e18** Response to Comment on Vandal et al. Insulin Reverses the High-Fat Diet–Induced Increase in Brain A β and Improves Memory in an Animal Model of Alzheimer Disease. *Diabetes* 2014;63:4291–4301
M. Vandal and F. Calon



The American Diabetes Association (ADA) is the nation's leading voluntary health organization supporting diabetes research, information, and advocacy. Its mission is to prevent and cure diabetes and to improve the lives of all people affected by diabetes. ADA is the leading publisher of comprehensive diabetes information. Its huge library of books and periodicals covers every aspect of diabetes and diabetes care.

To join ADA: Call 1-800-806-7801 or visit professional.diabetes.org/membership

To subscribe to ADA journals: Call 1-800-DIABETES or go to diabetesjournals.org

To order ADA books: Call 1-800-232-6733 or visit shopdiabetes.org

To access ADA's library of professional resources: Go to professional.diabetes.org

For more information about diabetes or ADA programs and services: Call 1-800-DIABETES. E-mail: AskADA@diabetes.org or visit diabetes.org

To locate an ADA/NCQA Recognized Provider of quality diabetes care in your area: Visit recognition.ncqa.org

To join the fight to increase funding for diabetes research, end discrimination, and improve insurance coverage:

Call 1-800-DIABETES or visit diabetes.org/advocacy

To find out how you can get involved with the programs in your community: Call 1-800-DIABETES or visit diabetes.org/in-my-community

To find out about important research regarding diabetes: Go to diabetes.org/research-and-practice

To make a donation or memorial contribution: Call 1-800-DIABETES or visit diabetes.org/donate