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**PERSPECTIVES IN DIABETES**

**1742** Indirect Regulation of Endogenous Glucose Production by Insulin: The Single Gateway Hypothesis Revisited  
R.N. Bergman and M.S. Iyer

**1748** Islet Encapsulation: Physiological Possibilities and Limitations  
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**1755** Ambient Air Pollution and Type 2 Diabetes: Do the Metabolic Effects of Air Pollution Start Early in Life?  
S.K. Park

**DIABETES SYMPOSIUM: EMERGING THERAPEUTIC TARGETS AND MECHANISMS OF ACTION**

This section features three articles from the 4th *Diabetes* Symposium held in conjunction with the ADA's 77th Scientific Sessions in San Diego, CA, 9–13 June 2017.

**1758** How Should We Think About the Role of the Brain in Glucose Homeostasis and Diabetes?  
J.D. Deem, K. Muta, J.M. Scarlett, G.J. Morton, and M.W. Schwartz

**1766** Single-Molecule Combinatorial Therapeutics for Treating Obesity and Diabetes  
M. Tschöp and R. DiMarchi

**1770** Mining the Genome for Therapeutic Targets  
J.C. Florez

**TECHNOLOGICAL ADVANCES**

**1779** Magnetic Resonance Neurography Visualizes Abnormalities in Sciatic and Tibial Nerves in Patients With Type 1 Diabetes and Neuropathy  
M. Vaeggemose, M. Pham, S. Ringgaard, H. Tankisi, N. Ejskjaer, S. Heiland, P.L. Poulsen, and H. Andersen

**METABOLISM**

**1789** Longitudinal Associations Between Ambient Air Pollution With Insulin Sensitivity,  $\beta$ -Cell Function, and Adiposity in Los Angeles Latino Children  
T.L. Alderete, R. Habre, C.M. Toledo-Corral, K. Berhane, Z. Chen, F.W. Lurmann, M.J. Weigensberg, M.I. Goran, and F.D. Gilliland

**1797** Hypothalamic and Striatal Insulin Action Suppresses Endogenous Glucose Production and May Stimulate Glucose Uptake During Hyperinsulinemia in Lean but Not in Overweight Men  
M. Heni, R. Wagner, S. Kullmann, S. Gancheva, M. Roden, A. Peter, N. Stefan, H. Preissl, H.-U. Häring, and A. Fritsche

**1807** Altered miR-29 Expression in Type 2 Diabetes Influences Glucose and Lipid Metabolism in Skeletal Muscle  
J. Massart, R.J.O. Sjögren, L.S. Lundell, J.M. Mudry, N. Franck, D.J. O'Gorman, B. Egan, J.R. Zierath, and A. Krook

**1819** NFE2 Induces miR-423-5p to Promote Gluconeogenesis and Hyperglycemia by Repressing the Hepatic FAM3A-ATP-Akt Pathway  
W. Yang, J. Wang, Z. Chen, J. Chen, Y. Meng, L. Chen, Y. Chang, B. Geng, L. Sun, L. Dou, J. Li, Y. Guan, Q. Cui, and J. Yang

**1833** Elov16 Deficiency Improves Glycemic Control in Diabetic *db/db* Mice by Expanding  $\beta$ -Cell Mass and Increasing Insulin Secretory Capacity  
H. Zhao, T. Matsuzaka, Y. Nakano, K. Motomura, N. Tang, T. Yokoo, Y. Okajima, S.-i. Han, Y. Takeuchi, Y. Aita, H. Iwasaki, S. Yatoh, H. Suzuki, M. Sekiya, N. Yahagi, Y. Nakagawa, H. Sone, N. Yamada, and H. Shimano

**1847** Hypoglycemic Effect of Combined Ghrelin and Glucagon Receptor Blockade  
B.K. Mani, A. Uchida, Y. Lee, S. Osborne-Lawrence, M.J. Charron, R.H. Unger, E.D. Berglund, and J.M. Zigman

**SIGNAL TRANSDUCTION**

**1858** Tumor Necrosis Factor- $\alpha$  Promotes Phosphoinositide 3-Kinase Enhancer A and AMP-Activated Protein Kinase Interaction to Suppress Lipid Oxidation in Skeletal Muscle  
M.C.L. Tse, O. Herlea-Pana, D. Brobst, X. Yang, J. Wood, X. Hu, Z. Liu, C.W. Lee, A.M. Zaw, B.K.C. Chow, K. Ye, and C.B. Chan

**OBESITY STUDIES**

**1871** Alterations in 3-Hydroxyisobutyrate and FGF21 Metabolism Are Associated With Protein Ingestion-Induced Insulin Resistance  
L.-A.L.S. Harris, G.I. Smith, B.W. Patterson, R.S. Ramaswamy, A.L. Okunade, S.C. Kelly, L.C. Porter, S. Klein, J. Yoshino, and B. Mittendorfer

**ISLET STUDIES**

**1879** Prolonged Elimination of Negative Feedback Control Mechanisms Along the Insulin Signaling Pathway Impairs  $\beta$ -Cell Function In Vivo  
R. Isaac, Y. Vinik, S. Boura-Halfon, L. Farack, S. Streim, E. Elhanany, Z. Kam, and Y. Zick

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Companion Article

- 1890** Kv2.1 Clustering Contributes to Insulin Exocytosis and Rescues Human  $\beta$ -Cell Dysfunction  
J. Fu, X. Dai, G. Plummer, K. Suzuki, A. Bautista, J.M. Githaka, L. Senior, M. Jensen, D. Greitzer-Antes, J.E. Manning Fox, H.Y. Gaisano, C.B. Newgard, N. Touret, and P.E. MacDonald
- 1901** Functional and Metabolomic Consequences of  $K_{ATP}$  Channel Inactivation in Human Islets  
C. Li, A.M. Ackermann, K.E. Boodhansingh, T.R. Bhatti, C. Liu, J. Schug, N. Doliba, B. Han, K.E. Cosgrove, I. Banerjee, F.M. Matschinsky, I. Nissim, K.H. Kaestner, A. Naji, N.S. Adzick, M.J. Dunne, C.A. Stanley, and D.D. De León
- 1914** GDF11 Attenuates Development of Type 2 Diabetes via Improvement of Islet  $\beta$ -Cell Function and Survival  
H. Li, Y. Li, L. Xiang, J. Zhang, B. Zhu, L. Xiang, J. Dong, M. Liu, and G. Xiang
- 1928** Genetic Disruption of Adenosine Kinase in Mouse Pancreatic  $\beta$ -Cells Protects Against High-Fat Diet-Induced Glucose Intolerance  
G. Navarro, Y. Abdolazami, Z. Zhao, H. Xu, S. Lee, N.A. Armstrong, and J.P. Annes

#### PATHOPHYSIOLOGY

- 1939** Renal and Vascular Effects of Uric Acid Lowering in Normouricemic Patients With Uncomplicated Type 1 Diabetes  
Y. Lytvyn, R. Har, A. Locke, V. Lai, D. Fong, A. Advani, B.A. Perkins, and D.Z.I. Cherney
- 1950** Identification of RUNX1 as a Mediator of Aberrant Retinal Angiogenesis  
J.D. Lam, D.J. Oh, L.L. Wong, D. Amarnani, C. Park-Windhol, A.V. Sanchez, J. Cardona-Velez, D. McGuone, A.O. Stemmer-Rachamimov, D. Elliott, D.R. Bielenberg, T. van Zyl, L. Shen, X. Gai, P.A. D'Amore, L.A. Kim, and J.F. Arboleda-Velasquez

#### COMPLICATIONS

- 1957** Metabolic Syndrome, Insulin Resistance, and Cognitive Dysfunction: Does Your Metabolic Profile Affect Your Brain?  
J.S. Neergaard, K. Dragsbæk, C. Christiansen, H.B. Nielsen, S. Brix, M.A. Karsdal, and K. Henriksen
- 1964** Heterogeneous Nuclear Ribonucleoprotein F Stimulates Sirtuin-1 Gene Expression and Attenuates Nephropathy Progression in Diabetic Mice  
C.-S. Lo, Y. Shi, I. Chenier, A. Ghosh, C.-H. Wu, J.-F. Cailhier, J. Ethier, J.-B. Lattouf, J.G. Filep, J.R. Ingelfinger, S.-L. Zhang, and J.S.D. Chan
- 1979** Impaired Glutamatergic Neurotransmission in the Ventromedial Hypothalamus May Contribute to Defective Counterregulation in Recurrently Hypoglycemic Rats  
G.M.I. Chowdhury, P. Wang, A. Ciardi, R. Mamillapalli, J. Johnson, W. Zhu, T. Eid, K. Behar, and O. Chan

- 1990** A Single Bout of High-Intensity Interval Training Reduces Awareness of Subsequent Hypoglycemia in Patients With Type 1 Diabetes  
H.M. Rooijackers, E.C. Wiegers, M. van der Graaf, D.H. Hijssen, R.P.C. Kessels, C.J. Tack, and B.E. de Galan
- 1999** Empagliflozin and Kinetics of Renal Glucose Transport in Healthy Individuals and Individuals With Type 2 Diabetes  
H. Al-Jobori, G. Daniele, E. Cersosimo, C. Triplitt, R. Mehta, L. Norton, R.A. DeFronzo, and M. Abdul-Ghani

#### PHARMACOLOGY AND THERAPEUTICS

- 2007** Neurturin and a GLP-1 Analogue Act Synergistically to Alleviate Diabetes in Zucker Diabetic Fatty Rats  
J.L. Trevaskis, C.B. Sacramento, H. Jouihan, S. Ali, J. Le Lay, S. Oldham, N. Bhagroo, B.B. Boland, J. Cann, Y. Chang, T. O'Day, V. Howard, C. Reers, M.S. Winzell, D.M. Smith, M. Feigh, P. Barkholt, K. Schreiter, M. Austen, U. Andag, S. Thompson, L. Jermutus, M.P. Coghlan, J. Grimsby, C. Dohrmann, C.J. Rhodes, C.M. Rondinone, and A. Sharma

#### GENETICS/GENOMES/PROTEOMICS/METABOLOMICS

- 2019** A Low-Frequency Inactivating *AKT2* Variant Enriched in the Finnish Population Is Associated With Fasting Insulin Levels and Type 2 Diabetes Risk  
A. Manning, H.M. Highland, J. Gasser, X. Sim, T. Tukiainen, and P. Fontanillas, et al.
- 2033** UBASH3A Mediates Risk for Type 1 Diabetes Through Inhibition of T-Cell Receptor-Induced NF- $\kappa$ B Signaling  
Y. Ge, T.K. Paisie, J.R.B. Newman, L.M. McIntyre, and P. Concannon
- 2044** Dominant ER Stress-Inducing *WFS1* Mutations Underlie a Genetic Syndrome of Neonatal/Infancy-Onset Diabetes, Congenital Sensorineural Deafness, and Congenital Cataracts  
E. De Franco, S.E. Flanagan, T. Yagi, D. Abreu, J. Mahadevan, M.B. Johnson, G. Jones, F. Acosta, M. Mulaudzi, N. Lek, V. Oh, O. Petz, R. Caswell, S. Ellard, F. Urano, and A.T. Hattersley
- 2054** Familial Hypercholesterolemia and Type 2 Diabetes in the Old Order Amish  
H. Xu, K.A. Ryan, T.J. Jaworek, L. Southam, J.G. Reid, J.D. Overton, A. Baras, M.K. Puurunen, E. Zeggini, S.I. Taylor, A.R. Shuldiner, and B.D. Mitchell

#### STATEMENT OF RETRACTION

- 2059** Statement of Retraction. EGFR Tyrosine Kinase Inhibitor (PD153035) Improves Glucose Tolerance and Insulin Action in High-Fat Diet-Fed Mice. *Diabetes* 2009;58:2910–2919. DOI: 10.2337/db08-0506. PMID: 19696185  
P.O. Prada, E.R. Ropelle, R.H. Mourão, C.T. de Souza, J.R. Pauli, D.E. Cintra, A. Schenka, S.A. Rocco, R. Rittner, K.G. Franchini, J. Vassallo, L.A. Velloso, J.B. Carvalheira, and M.J.A. Saad

#### ISSUES AND EVENTS

- 2060** Issues and Events

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*On the cover:* Fundus photograph of the right eye from a patient with proliferative diabetic retinopathy (surgeon's view). There are flame-shaped and dot blot hemorrhages within the retina as well as microaneurysms. Note the presence of a fibrovascular membrane extending from the optic nerve nasally, superiorly, and inferiorly causing a tractional retinal detachment superonasal to the optic nerve. In addition, there are retinal striae within the macula due to traction from the fibrovascular membrane. This fibrovascular membrane was surgically removed and evaluated via transcriptome analysis. This image is included in the Supplementary Data of an article in this issue by Lam et al., "Identification of RUNX1 as a Mediator of Aberrant Retinal Angiogenesis" (p. 1950). Photograph courtesy of Leo A. Kim, Massachusetts Eye and Ear, Harvard Medical School, Boston, MA.