

PERSPECTIVES IN DIABETES

β -Cell-specific gene repression: a mechanism to protect against inappropriate or maladjusted insulin secretion?

F. SCHUIT, L. VAN LOMMEL, M. GRANVIK, L. GOYVAERTS, G. DE FAUDEUR,
A. SCHRAENEN, AND K. LEMAIRE 969

COMMENTARIES

Paradigm shift or shifting paradigm for type 1 diabetes

M. NAKAYAMA AND G.S. EISENBARTH 976

PGC-1 α : the missing ingredient for mesenchymal stem cell-mediated angiogenesis

W.A. HSUEH AND A.A. GUPTA 979

Challenges of linking early-life conditions and disease susceptibility

F.H. EINSTEIN 981

Do acute exercise and diet reveal the molecular basis for metabolic flexibility in skeletal muscle?

B.H. GOODPASTER AND P.M. COEN 983

Selective insulin receptor modulators (SIRM): a new class of antidiabetes drugs?

R. VIGNERI, S. SQUATRITO, AND L. FRITITTA 984

GLP-1-based therapies and the exocrine pancreas: more light, or just more heat?

E.A.M. GALE 986

GLP-1 receptor agonist effects on normal and neoplastic pancreata

M. GOGGINS 989

Mitochondria, diabetes, and Alzheimer's disease

M. MILONE 991

A sweet new role for ubiquitin-specific protease 2 in controlling hepatic gluconeogenesis

B.N. FINCK 993

METHODOLOGY REVIEW

A novel method to measure glucose uptake and myosin heavy chain isoform expression of single fibers from rat skeletal muscle

J.G. MACKRELL AND G.D. CARTEE 995

METABOLISM

Concordance of changes in metabolic pathways based on plasma metabolomics and skeletal muscle transcriptomics in type 1 diabetes

T. DUTTA, H.S. CHAI, L.E. WARD, A. GHOSH, X.-M.T. PERSSON, G.C. FORD, Y.C. KUDVA, Z. SUN, Y.W. ASMANN, J.-P.A. KOCHER, AND K.S. NAIR 1004

The role of FOXO and PPAR transcription factors in diet-mediated inhibition of PDC activation and carbohydrate oxidation during exercise in humans and the role of pharmacological activation of PDC in overriding these changes

D. CONSTANTIN-TEODOSIU, D. CONSTANTIN, F. STEPHENS, D. LAITHWAITE, AND P.L. GREENHAFF 1017

Ubiquitin-specific protease 2 regulates hepatic gluconeogenesis and diurnal glucose metabolism through 11 β -hydroxysteroid dehydrogenase 1

M.M. MOLUSKY, S. LI, D. MA, L. YU, AND J.D. LIN 1025

Calorie restriction reduces the influence of glucoregulatory dysfunction on regional brain volume in aged rhesus monkeys

A.A. WILLETTE, B.B. BENDLIN, R.J. COLMAN, E.K. KASTMAN, A.S. FIELD, A.L. ALEXANDER, A. SRIDHARAN, D.B. ALLISON, R. ANDERSON, M.-L. VOYTKO, J.W. KEMNITZ, R.H. WEINDRUCH, AND S.C. JOHNSON 1036

Hypothalamic neuropeptide Y (NPY) controls hepatic VLDL-triglyceride secretion in rats via the sympathetic nervous system

E. BRUINSTROOP, L. PEI, M.T. ACKERMANS, E. FOPPEN, A.J. BORGERS, J. KWAKKEL, A. ALKEMADE, E. FLIERS, AND A. KALSBECK 1043

Loss of AMP-activated protein kinase- α 2 impairs the insulin-sensitizing effect of calorie restriction in skeletal muscle

P. WANG, R.-Y. ZHANG, J. SONG, Y.-F. GUAN, T.-Y. XU, H. DU, B. VIOLETT, AND C.-Y. MIAO 1051

Liver X receptor α is involved in the transcriptional regulation of the 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase gene

L.-F. ZHAO, Y. IWASAKI, M. NISHIYAMA, T. TAGUCHI, M. TSUGITA, M. OKAZAKI, S. NAKAYAMA, M. KAMBAYASHI, S. FUJIMOTO, K. HASHIMOTO, K. MURAO, AND Y. TERADA 1062

Deletion of the androgen receptor in adipose tissue in male mice elevates retinol binding protein 4 and reveals independent effects on visceral fat mass and on glucose homeostasis

K.J. MCINNES, L.B. SMITH, N.I. HUNGER, P.T.K. SAUNDERS, R. ANDREW, AND B.R. WALKER 1072

Diabetes-associated common genetic variation and its association with GLP-1 concentrations and response to exogenous GLP-1

G. SMUSHKIN, M. SATHANANTHAN, A. SATHANANTHAN, C. DALLA MAN, F. MICHELETTI, A.R. ZINSMEISTER, C. COBELLI, AND A. VELLA 1082

SIGNAL TRANSDUCTION

GLUT4 and glycogen synthase are key players in bed rest-induced insulin resistance

R.S. BIENSØ, S. RINGHOLM, K. KIILERICH, N.-J. AACHMANN-ANDERSEN, R. KROGH-MADSEN, B. GUERRA, P. PLUMGAARD, G. VAN HALL, J.T. TREEBAK, B. SALTIN, C. LUNDBY, J.A.L. CALBET, H. PILEGAARD, AND J.F.P. WOJASZEWSKI 1090

HDLs protect pancreatic β -cells against ER stress by restoring protein folding and trafficking

J. PÉTREMAND, J. PUYAL, J.-Y. CHATTON, J. DUPREZ, F. ALLAGNAT, M. FRIAS, R.W. JAMES, G. WAEBER, J.-C. JONAS, AND C. WIDMANN 1100

OBESITY STUDIES

Retinoic acid upregulates preadipocyte genes to block adipogenesis and suppress diet-induced obesity

D.C. BERRY, D. DESANTIS, H. SOLTANIAN, C.M. CRONIGER, AND N. NOY 1112

The role of liver fructose-1,6-bisphosphatase in regulating appetite and adiposity

S. VISINONI, N.F.I. KHALID, C.N. JOANNIDES, A. SHULKES, M. YIM, J. WHITEHEAD, T. TIGANIS, B.J. LAMONT, J.M. FAVALORO, J. PROIETTO, S. ANDRIKOPOULOS, AND B.C. FAM 1122

ISLET STUDIES

Transgenerational glucose intolerance with *Igf2/H19* epigenetic alterations in mouse islet induced by intrauterine hyperglycemia

G.-L. DING, F.-F. WANG, J. SHU, S. TIAN, Y. JIANG, D. ZHANG, N. WANG, Q. LUO, Y. ZHANG, F. JIN, P.C.K. LEUNG, J.-Z. SHENG, AND H.-F. HUANG 1133

Loss of HGF/c-Met signaling in pancreatic β -cells leads to incomplete maternal β -cell adaptation and gestational diabetes mellitus

C. DEMIRCI, S. ERNST, J.C. ALVAREZ-PEREZ, T. ROSA, S. VALLE, V. SHRIDHAR, G.P. CASINELLI, L.C. ALONSO, R.C. VASAVADA, AND A. GARCÍA-OCAÑA 1143

IMMUNOLOGY AND TRANSPLANTATION

Peroxisome proliferator-activated receptor- γ coactivator-1 α (PGC-1 α) enhances engraftment and angiogenesis of mesenchymal stem cells in diabetic hindlimb ischemia

D. LU, L. ZHANG, H. WANG, Y. ZHANG, J. LIU, J. XU, Z. LIANG, W. DENG, Y. JIANG, Q. WU, S. LI, Z. AI, Y. ZHONG, Y. YING, H. LIU, F. GAO, Z. ZHANG, AND B. CHEN 1153

Prevention of type 1 diabetes in the rat with an allele-specific anti-T-cell receptor antibody: V β 13 as a therapeutic target and biomarker

Z. LIU, L. CORT, R. EBERWINE, T. HERRMANN, J.H. LEIF, D.L. GREINER, B. YAHALOM, E.P. BLANKENHORN, AND J.P. MORDES 1160

Following the fate of one insulin-reactive CD4 T cell: conversion into Teffs and Tregs in the periphery controls diabetes in NOD mice

G. FOUSTERI, J. JASINSKI, A. DAVE, M. NAKAYAMA, P. PAGNI, F. LAMBOLEZ, T. JUNTTI, G. SARIKONDA, Y. CHENG, M. CROFT, H. CHEROUTRE, G. EISENBARTH, AND M. VON HERRATH 1169

Adoptive transfer with in vitro expanded human regulatory T cells protects against porcine islet xenograft rejection via interleukin-10 in humanized mice

S. YI, M. JI, J. WU, X. MA, P. PHILLIPS, W.J. HAWTHORNE, AND P.J. O'CONNELL 1180

Glycotoxin and autoantibodies are additive environmentally determined predictors of type 1 diabetes: a twin and population study		Peripheral blood monocyte gene expression profile clinically stratifies patients with recent-onset type 1 diabetes	
H. BEYAN, H. RIESE, M.I. HAWA, G. BERETTA, H.W. DAVIDSON, J.C. HUTTON, H. BURGER, M. SCHLOSSER, H. SNIEDER, B.O. BOEHM, AND R.D. LESLIE	1192	K.M. IRVINE, P. GALLEGOS, X. AN, S.E. BEST, G. THOMAS, C. WELLS, M. HARRIS, A. COTTERILL, AND R. THOMAS	1281
The radioprotective 105/MD-1 complex contributes to diet-induced obesity and adipose tissue inflammation		No interactions between previously associated 2-hour glucose gene variants and physical activity or BMI on 2-hour glucose levels	
Y. WATANABE, T. NAKAMURA, S. ISHIKAWA, S. FUJISAKA, I. USUI, K. TSUNEYAMA, Y. ICHIHARA, T. WADA, Y. HIRATA, T. SUGANAMI, H. IZAKI, S. AKIRA, K. MIYAKE, H.-o. KANAYAMA, M. SHIMABUKURO, M. SATA, T. SASAOKA, Y. OGAWA, K. TOBE, K. TAKATSU, AND Y. NAGAI	1199	R.A. SCOTT, A.Y. CHU, N. GRARUP, A.K. MANNING, M.F. HIVERT, D. SHUNGIN, A. TÖNYES, A. YESUPRIYA, D. BARNES, N. BOUATIA-NAJI, N.L. GLAZER, A.U. JACKSON, Z. KUTALIK, V. LAGOU, D. MAREK, L.J. RASMUSSEN-TORVIK, H.M. STRINGHAM, T. TANAKA, M. AADAHIL, D.E. ARKING, S. BERGMANN, E. BOERWINKLE, LL. BONNYCASTLE, S.R. BORNSTEIN, E. BRUNNER, S.J. BUMPSTEAD, S. BRAGE, O.D. CARLSON, H. CHEN, Y.-D.I. CHEN, P.S. CHINES, F.S. COLLINS, D.J. COUPER, E.M. DENNISON, N.F. DOWLING, J.S. EGAN, U. EKELUND, M.R. ERDOS, N.G. FOROUHI, C.S. FOX, M.O. GOODARZI, J. GRÄSSLER, S. GUSTAFSSON, G. HALLMANS, T. HANSEN, A. HINGORANI, J.W. HOLLOWAY, F.B. HU, B. ISOMAA, K.A. JAMESON, I. JOHANSSON, A. JONSSON, T. JØRGENSEN, M. KIVIMAKI, P. KOVACS, M. KUMARI, J. KUUSISTO, M. LAAKSO, C. LECOEUR, C. LÉVY-MARCHAL, G. LI, R.J.F. LOOS, V. LYSENKO, M. MARMOT, P. MARQUES-VIDAL, M.A. MORKEN, G. MÜLLER, K.E. NORTH, J.S. PANKOW, F. PAYNE, I. PROKOPENKO, B.M. PSATY, F. RENSTRÖM, K. RICE, J.I. ROTTER, D. RYBIN, C.H. SANDHOLT, A.A. SAYER, P. SHRADER, P.E.H. SCHWARZ, D.S. SISCOVICK, A. STANČÁKOVÁ, M. STUMVOLL, T.M. TESLOVICH, G. WAEBER, G.H. WILLIAMS, D.R. WITTE, A.R. WOOD, W. XIE, M. BOEHNKE, C. COOPER, L. FERRUCCI, P. FROGUEL, L. GROOP, W.H.L. KAO, P. VOLLENWEIDER, M. WALKER, R.M. WATANABE, O. PEDERSEN, J.B. MEIGS, E. INGELSSON, I. BARROSO, J.C. FLOREZ, P.W. FRANKS, J. DUPUIS, N.J. WAREHAM, AND C. LANGENBERG	1291
PATHOPHYSIOLOGY		Deep resequencing unveils genetic architecture of <i>ADIPOQ</i> and identifies a novel low-frequency variant strongly associated with adiponectin variation	
Short-term hyperinsulinemia and hyperglycemia increase myocardial lipid content in normal subjects		L.L. WARREN, L. LI, M.R. NELSON, M.G. EHM, J. SHEN, D.J. FRASER, J.L. APONTE, K.L. NANGLE, A.J. SLATER, P.M. WOOLLARD, M.D. HALL, S.D. TOPP, X. YUAN, L.R. CARDON, S.L. CHISSEOE, V. MOOSER, A.D. MORRIS, C.N.A. PALMER, J.R. PERRY, T.M. FRAYLING, J.C. WHITTAKER, AND D.M. WATERWORTH	1297
Y. WINHOFER, M. KRŠŠÁK, D. JANKOVIĆ, C.-H. ANDERWALD, G. REITER, A. HOFER, S. TRATTNIG, A. LUGER, AND M. KREBS	1210	COMPLICATIONS	
The WNT inhibitor Dickkopf 1 and bone morphogenetic protein 4 rescue adipogenesis in hypertrophic obesity in humans		ERRATUM	
B. GUSTAFSON AND U. SMITH	1217	PHARMACOLOGY AND THERAPEUTICS	
Diabetes disrupts the response of retinal endothelial cells to the angiomodulator lysophosphatidic acid		ISSUES AND EVENTS	
J. ARANDA, R. MOTIEJUNAITÉ, E. IM, AND A. KAZLAUSKAS	1225	DIABETES DIGESTS	
Metabolic alterations induced by sucrose intake and Alzheimer's disease promote similar brain mitochondrial abnormalities		ONLINE LETTERS TO THE EDITOR	
C. CARVALHO, S. CARDOSO, S.C. CORREIA, R.X. SANTOS, M.S. SANTOS, I. BALDEIRAS, C.R. OLIVEIRA, AND P.I. MOREIRA	1234	Comment on: Marquez et al. Low-frequency variants in <i>HMGA1</i> are not associated with type 2 diabetes risk. <i>Diabetes</i> 2012;61:524–530	
PHARMACOLOGY AND THERAPEUTICS		A. BRUNETTI, E. CHIEFARI, C.R. PULLINGER, S. TANYOLAC, D. FOTI, V. DURLACH, AND I.D. GOLDFINE	e3
The human GLP-1 analog liraglutide and the pancreas: evidence for the absence of structural pancreatic changes in three species			
N.C.B. NYBORG, A.-M. MØLK, L.W. MADSEN, AND L. BJERRE KNUDSEN	1243		
Chronic GLP-1 receptor activation by exendin-4 induces expansion of pancreatic duct glands in rats and accelerates formation of dysplastic lesions and chronic pancreatitis in the <i>Kras</i> ^{G12D} mouse model			
B. GIER, A.V. MATVEYENKO, D. KIRAKOSSIAN, D. DAWSON, S.M. DRY, AND P.C. BUTLER	1250		
A fully human, allosteric monoclonal antibody that activates the insulin receptor and improves glycemic control			
V. BHASKAR, I.D. GOLDFINE, D.H. BEDINGER, A. LAU, H.F. KUAN, L.M. GROSS, M. HANNA, B.A. MADDUX, S.R. WATSON, S. ZHU, A.J. NARASIMHA, R. LEVY, L. WEBSTER, S.D. WIJESURIYA, N. LIU, X. WU, D. CHEMLA-VOGEL, C. TRAN, S.R. LEE, S. WONG, D. WILCOCK, M.L. WHITE, AND J.A. CORBIN	1263		
GENETICS/GENOMES/PROTEOMICS/METABOLOMICS			
Placental adiponectin gene DNA methylation levels are associated with mothers' blood glucose concentration			
L. BOUCHARD, M.-F. HIVERT, S.-P. GUAY, J. ST-PIERRE, P. PERRON, AND D. BRISSON	1272		