MINI-REVIEWS

DIABETES, PANCREATIC AND GASTROINTESTINAL HORMONES

1049  The Diverse Metabolic Roles of Peripheral Serotonin
       Alyce M. Martin, Richard L. Young, Lex Leong, Geraint B. Rogers, Nick J. Spencer, Claire F. Jessup, and Damien J. Keating
       Précis: Review of the emerging endocrine roles of peripheral serotonin.

1064  Impaired "Glycine"-mia in Type 2 Diabetes and Potential Mechanisms Contributing to Glucose Homeostasis
       Richard Yan-Do and Patrick E. MacDonald
       Précis: Glycine is a potential biomarker for type 2 diabetes. The contribution of reduced glycine to impaired glucose control remains unclear. We review potential impacts in the brain, pancreas, and elsewhere.

1074  Glucose Homeostasis: Regulation by Peripheral Circadian Clocks in Rodents and Humans
       Frédéric Gachon, Ursula Loizides-Mangold, Volodymyr Petrenko, and Charna Dibner
       Précis: This review summarizes recent findings on the molecular and cellular makeup of the circadian timing system and its implications in temporal coordination of glucose metabolism in health and disease.

ENERGY BALANCE - OBESITY - METABOLISM

1085  Novel Hypothalamic Mechanisms in the Pathophysiological Control of Body Weight and Metabolism
       Diego Perez-Tilve
       Précis: This review summarizes recent findings about the role of the central nervous system in the control of energy balance.

1095  Sex Hormones and Cardiometabolic Health: Role of Estrogen and Estrogen Receptors
       Deborah Clegg, Andrea L. Hevener, Kerrie L. Moreau, Eugenia Morselli, Alfredo Criollo, Rachael E. Van Pelt, and Victoria J. Vieira-Potter
       Précis: A brief detailed overview of the literature from basic science to human clinical trials supporting a protective role of estrogens, specifically signaling through ERα, in cardiometabolic health.

NEWS AND VIEWS

CALCIUM METABOLISM - BONE

1106  PTH Regulation of FGF23 Fragments: A Tail in Two Acts (For article see page 1130)
       Larry J. Suva and Peter A. Friedman
ENERGY BALANCE - OBESITY - METABOLISM

1109  Getting the Skinny on Follistatin and Fat  (For article see page 1217)
    Jia-Xu Li and Carolyn L. Cummins

1113  Chewing the Fat: A Metabolic Role for Ldb1 Beyond the Pancreas?  (For article see page 1289)
    Emily K. Sims

THYROID FUNCTION AND REGULATION

1116  Beam Me In: Thyroid Hormone Analog Targets Alternative Transporter in Mouse Model of X-Linked Adrenoleukodystrophy  (For article see page 1328)
    Anna Milanesi and Gregory A. Brent

RAPID COMMUNICATION

ENERGY BALANCE - OBESITY - METABOLISM

1120  Neurosecretory Protein GL, a Hypothalamic Small Secretory Protein, Participates in Energy Homeostasis in Male Mice
    Daichi Matsuura, Kenshiro Shikano, Takaya Saito, Eiko Iwakoshi-Ukena, Megumi Furumitsu, Yuta Ochi, Manami Sato, George E. Bentley, Lance J. Kriegsfeld, and Kazuyoshi Ukena

RESEARCH ARTICLES

CALCIUM METABOLISM - BONE

1130  Acute Parathyroid Hormone Injection Increases C-Terminal but Not Intact Fibroblast Growth Factor 23 Levels  (For News and Views see page 1106)
    Vanessa M. Knab, Braden Corbin, Olena Andrukhova, Julia M. Hum, Pu Ni, Seham Rabadi, Akira Maeda, Kenneth E. White, Reinhold G. Erben, Harald Jüppner, and Marta Christov

DEVELOPMENT

1140  Hepatic Insulin Resistance and Altered Gluconeogenic Pathway in Premature Baboons
    Lisa McGill-Vargas, Amalia Gastaldelli, Hanyu Liang, Diana Anzueto Guerra, Teresa Johnson-Pais, Steven Seidner, Donald McCurnin, Giovanna Muscogiuri, Ralph DeFronzo, Nicolas Musi, and Cynthia Blanco

DEVELOPMENTAL BASIS OF ADULT DISEASE

1152  Assisted Reproductive Technologies Predispose to Insulin Resistance and Obesity in Male Mice Challenged With a High-Fat Diet
    David Cerny, Claudio Sartori, Stefano F. Rimoldi, Théo Meister, Rodrigo Sonia, Elisa Bouillet, Urs Scherrer, and Emrush Rexhaj

DIABETES - INSULIN - GLUCAGON - GASTROINTESTINAL

1160  Whole-Body Vibration Mimics the Metabolic Effects of Exercise in Male Leptin Receptor–Deficient Mice

Précis: We compared the effects of exercise and whole-body vibration in obese and nonobese mice. The results indicate that whole-body vibration mimics the effects of exercise on metabolism in obese mice.
DIABETES, PANCREATIC AND GASTROINTESTINAL HORMONES

1172 Long-Chain Free Fatty Acid Receptor GPR120 Mediates Oil-Induced GIP Secretion Through CCK in Male Mice
Akiko Sankoda, Norio Harada, Kanako Iwasaki, Shunsuke Yamane, Yuki Murata, Kimitaka Shibue, Yotsapon Thewjitcharoen, Kazuyo Suzuki, Takanari Harada, Yoshinori Kanemaru, Satoko Shimazu-Kuivahara, Akira Hirasawa, and Nobuya Inagaki

Precis: GPR120 contributes to oil-induced GIP secretion in mice by enhancing CCK secretion, whereas GPR40 contributes more greatly and is involved in both CCK-dependent and -independent GIP secretion in vivo.

ENDOCRINE ORGAN PHYSIOLOGY AND PATHOPHYSIOLOGY

1181 Hyperhomocysteinemia Promotes Insulin Resistance and Adipose Tissue Inflammation in PCOS Mice Through Modulating M2 Macrophage Polarization via Estrogen Suppression
Xinyu Qi, Bochun Zhang, Yue Zhao, Rong Li, Hsun-Ming Chang, Yanli Pang, and Jie Qiao

Precis: Treatment of female mice with DHEA induced PCOS-like symptoms. HHcy may exaggerate IR in the PCOS-like mice, most likely via the estrogen-mediated imbalance of macrophage M1/M2 polarization.

ENERGY BALANCE - OBESITY - METABOLISM

1194 Endogenous Calcitonin Gene-Related Peptide Regulates Lipid Metabolism and Energy Homeostasis in Male Mice
Tian Liu, Akiko Kamiyoshi, Takayuki Sakurai, Yuka Ichikawa-Shindo, Hisaka Kawate, Lei Yang, Megumu Tanaka, Xian Xian, Akira Inai, Liuyu Zhai, Kazutaka Hirabayashi, Kun Dai, Keiya Tamamura, Teng Liu, Nanqi Cui, Kyoko Igarashi, Akhiro Yamauchi, and Takayuki Shindo

Precis: Effects of CGRP on metabolic function were analyzed using CGRP^{−/−}, which showed resistance to obesity with higher expression of β3-adrenergic receptor and higher glycerol release from adipose tissue.

1207 Liver NF-κB-Inducing Kinase Promotes Liver Steatosis and Glucose Counterregulation in Male Mice With Obesity
Yan Liu, Liang Sheng, Yi Xiong, Hong Shen, Yong Liu, and Liangyou Rui

Precis: NIK was conditionally deleted in mice. Deletion of NIK in the liver but not hepatocytes or immune cells alone protects against HFD-induced liver steatosis and hepatic glucose production.

1217 Follistatin Targets Distinct Pathways To Promote Brown Adipocyte Characteristics in Brown and White Adipose Tissues (For News and Views see page 1109)

Precis: Follistatin promotes brown adipocyte characteristics by targeting distinct pathways in white and brown adipose tissues.

1231 Hypoxia-Inducible Lipid Droplet–Associated Is Not a Direct Physiological Regulator of Lipolysis in Adipose Tissue
Wieneke Dijk, Frits Mattijsen, Montserrat de la Rosa Rodriguez, Angel Loza Valdes, Anne Loft, Susanne Mandrup, Eric Kalkhoven, Ling Qi, Jan Willem Borst, and Sander Kersten

Precis: We found, using in vivo and in vitro gene silencing and overexpression, that the lipid droplet–associated protein HILPDA is not a physiological regulator of adipocyte lipolysis.

1252 ANGPTL8 Blockade With a Monoclonal Antibody Promotes Triglyceride Clearance, Energy Expenditure, and Weight Loss in Mice
Viktoria Gusarova, Serena Banfi, Corey A. Alexo-Braun, Lisa M. Shihanian, Ivory J. Mintah, Joseph S. Lee, Yurong Xin, Qi Su, Vishal Kamat, Jonathan C. Cohen, Helen H. Hobbs, Brian Zambrowicz, George D. Yancopoulos, Andrew J. Murphy, and Jesper Gronrved

Precis: This study describes a specific and efficacious blocking monoclonal antibody to ANGPTL8 that lowers circulating triglycerides in mice and nonhuman primates.

1260 Short-Term Versus Long-Term Effects of Adipocyte Toll-Like Receptor 4 Activation on Insulin Resistance in Male Mice
Caroline Tao, William L. Holland, Qiong A. Wang, Mengle Shao, Lin Jia, Kai Sun, Xiaoli Lin, Yi-Chun Kuo, Joshua A. Johnson, Ruth Gordillo, Joel K. Elmqist, and Philipp E. Scherer

Precis: Lack of adipocyte TLR4 signaling gives rise to a complex metabolic phenotype with improved resistance to acute exposure to saturated fats, whereas it is detrimental upon prolonged HFD exposure.
Loss of Action via Neurotensin-Leptin Receptor Neurons Disrupts Leptin and Ghrelin-Mediated Control of Energy Balance
Juliette A. Brown, Raluca Bugescu, Thomas A. Mayer, Adriana Gata-Garcia, Gizem Kurt, Hillary L. Woodworth, and Gina M. Leinninger

Precis: We investigated how energy cues engage the lateral hypothalamus, and reveal that leptin-sensing neurotensin neurons are hubs for hormone-mediated control of ingestive and locomotor behaviors.

LDB1 Regulates Energy Homeostasis During Diet-Induced Obesity (For News and Views see page 1113)
Christine Loyd, Yanping Liu, Teayoun Kim, Cassie Holleman, Jamie Galloway, Maigen Bethea, Benjamin N. Ediger, Thomas A. Swain, Doris A. Stoffers, Glenn C. Rowe, Martin Young, Chad Steele, Kirk M. Habegger, and Chad S. Hunter

Precis: We report that the Ldb1 transcriptional coregulator has roles in energy homeostasis, in part through transcriptional modulation of critical regulators of brown adipose tissue function.

A Selective Bombesin Receptor Subtype 3 Agonist Promotes Weight Loss in Male Diet-Induced–Obese Rats With Circadian Rhythm Change
Yasunori Nio, Natsu Hotta, Minoru Maruyama, Kenichi Hamagami, Toshimi Nagi, Masaaki Funata, Junichi Sakamoto, Masanori Nakakaniya, Nobuyuki Amano, Tomohiro Okawa, Yasuyoshi Arikawa, Shinobu Sasaki, Shoki Okuda, Shizuo Kasai, Yugo Habata, and Yasutaka Nagisa

Precis: We identified a novel BRS-3 agonist, compound-A, and possible mechanism of antiobesity effects modulating circadian rhythm and activation of the HPA axis via SCN.

PROTEIN TRANSLATION AND MODIFICATION

A Novel Fc-FGF21 With Improved Resistance to Proteolysis, Increased Affinity Toward β-Klotho, and Enhanced Efficacy in Mice and Cynomolgus Monkeys
Shanaka Stanislaus, Randy Hecht, Junming Yie, Todd Hager, Michael Hall, Chris Spahr, Wei Wang, Jennifer Weiszmann, Yang Li, Liying Deng, Dwight Winters, Stephen Smith, Lei Zhou, Yuesheng Li, Murielle M. Veniant, and Jing Xu

Precis: An engineered FGF21 with improved pharmacokinetic, pharmacodynamic, and pharmaceutical properties was developed for the treatment of type 2 diabetes and obesity.

THYROID FUNCTION AND REGULATION

A Thyroid Hormone–Based Strategy for Correcting the Biochemical Abnormality in X-Linked Adrenoleukodystrophy (For News and Views see page 1116)
Meredith D. Hartley, Lisa L. Kirkemo, Tapasree Banerji, and Thomas S. Scanlan

Precis: Thyroid hormone and the thyromimetic sobetirome lower CNS levels of very long chain fatty acids in a mouse model of X-linked adrenoleukodystrophy supporting a therapeutic strategy for X-ALD.

ADDITIONAL RESEARCH ARTICLES

ADRENAL FUNCTION AND REGULATION

Postnatal Ontogeny of the Circadian Expression of the Adrenal Clock Genes and Corticosterone Rhythm in Male Rats
Silvia Liliana Ruiz Roa, Edson Zangiacomi Martinez, Clarissa Silva Martins, Sonir Rauber Antonini, Margaret de Castro, and Ayrton Custódio Moreira

Precis: In rat adrenals, the assessment of clock genes expression ontogeny revealed a progressive postnatal maturation of clock genes circadian variation in synchrony with corticosterone circadian rhythm.

CALCIUM METABOLISM - BONE

Molecular Physiology of the Hypocalcemic Action of Fibroblast Growth Factor 23 in Zebrafish (Danio rerio)
Chia-Hao Lin, Huei-Jyun Hu, and Pung-Pung Hwang

Precis: FGF23 and calcium regulation in zebrafish.
DEVELOPMENTAL BASIS OF ADULT DISEASE

1359  Vasoprotective Activities of the Adrenomedullin-RAMP2 System in Endothelial Cells
Xian Xian, Takayuki Sakurai, Akiko Kamiyoshi, Yuka Ichikawa-Shindo, Megumu Tanaka, Teruhide Koyama, Hisaka Kawate, Lei Yang, Tian Liu, Akira Imai, Liuyu Zhai, Kazutaka Hirabayashi, Kun Dai, Keiya Tanimura, Teng Liu, Nanqi Cui, Kyoko Igarashi, Akhiro Yamauchi, and Takayuki Shindo

Précis: We assessed the actions of the AM-RAMP2 system using a vascular injury model and demonstrated this system exerts vasoprotective effects and is a novel therapeutic target for vascular diseases.

DIABETES - INSULIN - GLUCAGON - GASTROINTESTINAL

1373  Vessel Network Architecture of Adult Human Islets Promotes Distinct Cell-Cell Interactions In Situ and Is Altered After Transplantation

Précis: Three-dimensional analysis revealed that endogenous human islets exhibit a distinct vascular network that promotes specific cell-cell interactions of islet cells and substantially alters after transplantation.

GROWTH HORMONES - GROWTH FACTORS

1386  Activation of Male Liver Chromatin Accessibility and STAT5-Dependent Gene Transcription by Plasma Growth Hormone Pulses
Jeannette Connerney, Dana Lau-Corona, Andy Rampersaud, and David J. Waxman

Précis: Igf1, Cish, and a subset of male-biased liver genes undergo rapid pulsatile increases in chromatin accessibility and gene transcription with each male plasma GH pulse-induced cycle of STAT5 activation.

1406  Insulin, IGF-1, and GH Receptors Are Altered in an Adipose Tissue Depot–Specific Manner in Male Mice With Modified GH Action
Rikke Hjortebjerg, Darlene E. Benryman, Ross Comisford, Stuart J. Frank, Edward O. List, Mette Bjerre, Jan Frystyk, and John J. Kopchick

Précis: This article shows that the expressions of GH, IGF-1, and insulin receptors in mouse AT are affected by modified GH action. Furthermore, receptor expressions occur in a depot-dependent manner.

NEUROENDOCRINOLOGY

1419  Protective Effects of Fetal Zone Steroids Are Comparable to Estradiol in Hyperoxia–Induced Cell Death of Immature Glia
Stephanie Hübner, Donna E. Sunny, Christine Pohlke, Johanna Ruhnau, Antje Vogelgesang, Bettina Reich, and Matthias Heckmann

Précis: Fetal zone steroid (FZS)–mediated neuroprotection was similar to that of E2 in a preterm hyperoxia model. In the presence of FZSs, there was no synergism with E2 treatment in two of three cell types.

1436  Circulating Ghrelin Acts on GABA Neurons of the Area Postrema and Mediates Gastric Emptying in Male Mice
Agustina Cabral, María P. Cornejo, Gimena Fernandez, Pablo N. de Francesco, Guadalupe García-Romero, Maia Uriarte, Jeffrey M. Zigman, Enrique Portiansky, Mirta Reynaldo, and Mario Perello

Précis: The capacity of circulating ghrelin to induce gastric emptying in mice requires the integrity of the area postrema, which contains a population of GABA neurons that are the target of plasma ghrelin.

PITUITARY

1450  Elucidating the Role of the Desmosome Protein p53 Apoptosis Effector Related to PMP-22 in Growth Hormone Tumors
Katja Kiseljak-Vassiliades, Taylor S. Mills, Yu Zhang, Mei Xu, Kevin O. Lillehei, B. K. Kleinschmidt-DeMasters, and Margaret E. Wierman

Précis: PERP and desmosome components are dysregulated in sparsely granulated GH tumors. In vitro studies suggest that downregulation of PERP plays an important role in sparsely granulated tumorigenesis and survival.
REPRODUCTION, SEX, AND GENDER

1461 Demonstration of a Functional Kisspeptin/Kisspeptin Receptor System in Amphioxus With Implications for Origin of Neuroendocrine Regulation
Peng Wang, Meng Wang, Guangdong Ji, Shuangshuang Yang, Shicui Zhang, and Zhenhui Liu
Précis: The Kiss-Kissr system was identified in amphioxus. Kiss can interact with Kissr, induce zebrafish LH release, and increase amphioxus gp5 expression. Also, Kiss/Kissr is down-regulated after spawning.

1474 The Steroid Metabolome in the Isolated Ovarian Follicle and Its Response to Androgen Exposure and Antagonism
Marie Lebbe, Angela E. Taylor, Jenny A. Visser, Jackson C. Kirkman-Brown, Teresa K. Woodruff, and Wiebke Arlt
Précis: Steroid metabolome analysis by mass spectrometry in the isolated ovarian follicle revealed early developmental capacity for androgen synthesis, which was upregulated by androgen receptor antagonists.

STEROID HORMONE ACTIONS

1486 Genome-Wide Identification of Basic Helix–Loop–Helix and NF-1 Motifs Underlying GR Binding Sites in Male Rat Hippocampus
Précis: A stressful experience does not influence GR binding in the hippocampus relative to nonstressed controls. Insights into GR binding mechanisms include support via basic helix–loop–helix and NF-1 motifs.

THYROID FUNCTION AND REGULATION

1502 N-Acetylcysteine Prevents Low T3 Syndrome and Attenuates Cardiac Dysfunction in a Male Rat Model of Myocardial Infarction
Tatiana Ederich Lehnhen, Marcus Vinicius Santos, Adrio Lima, Ana Luiza Maia, and Simone Magagnin Wajner
Précis: Restoring redox balance by NAC treatment prevents NTIS-related thyroid hormone derangement and preserves heart function in rats subjected to MI.

TRANScription - GENE REGULATION

1511 NeuroD Factors Discriminate Mineralocorticoid From Glucocorticoid Receptor DNA Binding in the Male Rat Brain
Lisa T.C.M. van Weert, Jacobus C. Buurstede, Ahmed Mahfouz, Pamela S.M. Braakhuis, J. Annelies E. Polman, Hetty C.M. Sips, Benno Roozendaal, Judith Balog, E. Ronald de Kloet, Nicole A. Datson, and Onno C. Meijer
Précis: Genome-wide identification of corticosteroid receptor binding loci on the DNA suggests that at MR-exclusive binding sites, NeuroD factors cooperate with MR binding and/or functionality.

LETTER TO THE EDITOR

1523 Letter to the Editor: Parameters, Characteristics, and Criteria for Defining the Term “FGF21 Resistance”
Pongpan Tanajak

CORRECTIONS

1525 Erratum for “Anti-Opioid Effects of RFRP-3 on Magnocellular Neuron Activity in Morphine-Naïve and Morphine-Treated Female Rats?”

ENDOCRINE SOCIETY

1A Society page
2A Masthead
3A Editorial Board
17A Forthcoming Articles
18A Checklist & Guidelines
20A Author Guidelines
1B JCEM Table of Contents Snapshot
3B Journal of the Endocrine Society Table of Contents Snapshot

Cover