



Mitochondrial uncoupling proteins and obesity: Molecular and genetic aspects of UCP1

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Genetic variation in brown fat specific mitochondrial uncoupling protein-1 (UCP1) expression and brown adipocyte morphology, have provided models to test the hypothesis that nonshivering thermogenesis is associated with the regulation of body weight. Genetic manipulation using transgenic animals and gene targeting, has resulted in mice with an over-expression of UCP1. These variant animals consistently show that over-expression of UCP1 reduced adiposity. On the other hand, less agreement is found in models that reduce nonshivering thermogenesis. Inactivation of the UCP1 gene, by gene targeting, does not increase adiposity when compared to control animals; however, a mouse expressing the UCP1-DTA transgene (UCP1-diphtheria toxin A chain), in which there is a modest reduction in the number of brown adipocytes, becomes obese. Other phenotypes of this mouse, the hyperphagia, extreme resistance to leptin administration, retinopathy and high residual content of brown adipocytes, suggest that the effects of the transgene may be more extensive than simply a 60% reduction in the number of brown adipocytes. Ectopic expression of UCP1-DTA in the brain could explain the phenotype of this mouse in a manner more consistent with the results of other models with altered UCP1 and brown adipocyte expression.

Keywords: transgene; UCP-DTA; α P2-UCP1; UCP1-KO; PGC1; brown adipose tissue

Introduction

Experimental manipulations of brown adipose tissue (BAT) with genetic and pharmacological techniques in several animal models, have provided strong evidence that an increase in nonshivering thermogenesis is an effective mechanism for the regulation of body weight. Reductions in the capacity for thermogenesis, generally lead to increased adiposity, while an increased thermogenic capacity reduces adiposity. Although the experimental evidence from these studies strongly support a role for the brown fat specific mitochondrial uncoupling protein (UCP1) as the principle thermogenic mechanism causing a change in adiposity, it is possible that some of the effects are due to other thermogenic mechanisms. Of particular interest is the need to evaluate the role the other members in the UCP family of genes the thermogenic processes involved in the regulation of body weight.¹⁻⁵ For example, mice in which the *Ucp1* gene has been inactivated by gene targeting, are sensitive to cold, but they are not more obese than the control mice that have a fully functioning *Ucp1* gene.⁶ Since the UCP1-deficient mice have elevated levels of UCP2 mRNA,

it has been suggested that UCP2 compensates for the loss of UCP1 in maintaining a normal body weight.⁶ However, if UCP2 is able to compensate for UCP1 in regulating body weight, then why does it not compensate for *Ucp1* deficiency in protecting mice from acute exposure to cold? Our ability to detect these relationships is dependent on several parameters, including genetic background, gender and age. Of particular importance is the genetic background of the animal, since this can influence the development of obesity by variant genes that are independent of nonshivering thermogenesis. The interaction of other variant genes can affect thermogenesis and have a large impact on the response of the animal to beta adrenergic agonists. It is important to emphasize that for a genetically defined model of obesity like diet-induced obesity of the A/J and C57BL/6J inbred strains,⁷ the susceptibility to obesity is almost certainly the consequence of the interactions of several sub-phenotypes and each of these sub-phenotypes will be determined by several genes. Given our focused agenda, we will discuss only the genetic variation associated with UCP1.

Knockout and transgenic models

We would like to review the genetic evidence that elevated UCP1 concentrations increase energy expenditure, with a resulting reduction in adiposity and, conversely, that reduced UCP1 leads to increased adiposity. The first genetic study to address this

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Molecular And Genetic Aspects Of Obesity

Gabriel I. Uwaifo



Molecular And Genetic Aspects Of Obesity:

Molecular and Genetic Aspects of Obesity Pennington Biomedical Research Foundation, 1996 Covers genetic models of obesity the biology of animal models used in the research the regulation of food intake adipose tissue the genetics of human obesity molecular markers and transgenic models The 37 papers from a symposium in Baton Rouge in February 1994 are informed by two recent dev Handbook of Eating Disorders and Obesity Stephan Herpertz, Martina de Zwaan, Stephan Zipfel, 2024-04-24 This book covers the entire spectrum of eating disorders including obesity in a psychotherapy procedure independent manner and is based on the latest treatment guidelines All disorders are presented on the basis of current evidence and treatment guidelines that combine psychotherapeutic and pharmacological interventions to provide therapists with clear recommendations for treatment The 3rd edition has been completely revised to include important current topics and chapters such as the inclusion of eating disorders in ICD 11 DSM 5 the role of the microbiome and the role of modern media e g ehealth in prevention and treatment In addition the editors and authors address among other topics systemic therapy as a new evidence based psychotherapy and the discussion of addiction mechanisms in eating and weight disorders and provide an outlook on the role of neurostimulation procedures to address current developments in obesity and eating disorders The book is suitable as a reference for physicians in training educators and psychologists especially colleagues from the field of psychosomatics psychiatrists and psychotherapists in research clinic and practice The Human Hypothalamus Gabriel I. Uwaifo, 2020-12-24 The hypothalamus is an anatomically small but functionally important part of the brain In functional and pathophysiological terms the hypothalamus represents the intersection of several areas of clinical and medical expertise The human hypothalamus can be astutely referred to as the crossroad of endocrinology psychiatry neurology and neurosurgery Because of its involvement in myriad physiologic functions and the varied ways disorders involving it can manifest hypothalamic disease can initially come to medical attention in widely disparate settings and with widely different clinicians Therefore the detection and proper care of hypothalamic dysfunction and disease often requires carefully coordinated multidisciplinary care This volume fills a significant void in the medical professional community comprehensively presenting the scope of hypothalamic structure function dysfunction and disease to cater to the various clinical teaching and research professionals that have a stake in this part of the human brain This text captures in one place all the information that practicing clinicians clinician scientists and researchers need to be adequately informed about various aspects of the hypothalamus in all its complexity It is comprehensive and broad in scope so that it provides relevant reference information for the wide range of professionals involved in the pre and post mortem detection diagnosis characterization care and management of various hypothalamic disorders and diseases in addition to providing a sound anatomic and physiologic foundation of the normal human hypothalamus The Human Hypothalamus can be used to differing degrees by medical professionals and students alike finding utility for interested general clinicians medical school and allied

health professional teaching faculty as well as subspecialists in domains as wide as neurosurgery neuroendocrinology clinical psychiatry and neuro oncology *Molecular Biomarkers In Cardiology* Pietro Scicchitano,2021-04-28 ear Colleagues The approach to diseases is facing novel frontiers targeting gene and improving person centered medicine able to easily and specifically detect early stages of pathologies The present book includes the most futuristic approaches to the identification of cardiac diseases by means of the most recent discoveries in molecular and genetic diagnosis The articles will give you the opportunity to think of cardiac diseases as adverse conditions which can be more easily detected by means of technologies and the research spirit of us physicians dedicated to humans care Please enjoy this reading *Bibliography of Agriculture* ,1998 **Genetic Diagnosis of Endocrine Disorders** Roy E. Weiss,Samuel Refetoff,2015-10-09 Genetic Diagnosis of Endocrine Disorders Second Edition provides users with a comprehensive reference that is organized by endocrine grouping i e thyroid pancreas parathyroid pituitary adrenal and reproductive and bone discussing the genetic and molecular basis for the diagnosis of various disorders The book emphasizes the practical nature of diagnosing a disease including which tests should be done for the diagnosis of diabetes mellitus in adults and children which genes should be evaluated for subjects with congenital hypothyroidism which genetic tests should be ordered in obese patients or for those with parathyroid carcinoma and the rationale behind testing for multiple endocrine neoplasias Offers a clear presentations of pharmacogenetics and the actual assays used in detecting endocrine diseases Teaches the essentials of the genetic basis of disease in each major endocrine organ system Offers expert advice from genetic counselors on how to use genetic information in counseling patients Includes new chapters on the genetics of lipid disorders and glycogen storage diseases genetics of hypoglycemia and whole genome exome sequencing *Genetic Variation and Nutrition* A. P. Simopoulos,B. Childs,1990-06-20 **Textbook of Obesity** Sharon R. Akabas,Sally Ann Lederman,Barbara J. Moore,2012-05-08 Textbook of Obesity is designed to cover all of the essential elements concerning the etiology prevention and treatment of obesity suitable for students in nutrition dietetics and health science courses Providing core knowledge for students is an essential and urgent requirement to ensure that those graduating will be properly equipped to deal with the high prevalence of overweight and obesity currently affecting almost two thirds of the population of the USA and with prevalence in much of the rest of the world rapidly catching up This landmark text is organized into 5 parts comprising 27 chapters each carefully written in a user friendly style by experts in the area Part I helps the reader to understand the scope and complexity of the problem of obesity Part II focuses on obesity etiology Part III examines the health consequences of obesity for both children and adults Part IV discusses the challenge of assessing obesity in humans and offers insights into community factors that influence the risk of obesity Finally Part V dedicates 13 chapters to a discussion of a wide variety of obesity prevention and treatment interventions that are currently in use Textbook of Obesity is an essential purchase for students and the many health professionals dealing with obesity on a day to day basis A dedicated companion website features an extensive bank of

questions and answers for readers to test their understanding and all of the book's illustrations for instructors to download www.wiley.com/go/akabasobesity

Human Body Composition Steven Heymsfield, 2005 The 2nd edition of Human Body Composition includes updated information and new chapters The editors and 35 contributors are well respected researchers in the field of body composition science This is one of few texts that provides comprehensive coverage of body composition research The primary intent is to present current information on research methods This book can serve as a textbook for those who are students or new researchers Descriptions of various methods and background information are imparted in great detail with numerous references New chapters address energy expenditure animal body composition molecular genetics and body composition as it relates to disease states of cancer HIV obesity and certain inflammatory diseases like rheumatoid arthritis inflammatory bowel disease congestive heart failure and chronic obstructive pulmonary disease This book is recommended for students and new researchers in the field of body composition research who need to learn various methods histories and practical applications Publisher's description

Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults (U.S.), 1998 Of evidence based recommendations Introduction Overweight and obesity background Examination of randomized controlled trial evidence Treatment guidelines Summary of recommendations Future research

Biomedical Index to PHS-supported Research: pt. A. Subject access A-H, 1992

Eating Disorders and Obesity Christopher G. Fairburn, Kelly D. Brownell, 2005-07-01 This unique handbook presents and integrates virtually all that is currently known about eating disorders and obesity in one authoritative accessible and eminently practical volume From leading international authorities 112 concise chapters encapsulate the latest information on all pertinent topics from biological psychological and social processes associated with risk to clinical methods for assessment and intervention The contents are organized to highlight areas of overlap between lines of research that often remain disparate Suggestions for further reading at the end of each chapter replace extended references and enhance the practical value and readability of the volume

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Hypothalamic Integration of Energy Metabolism A. Kalsbeek, Eric Fliers, Michel A. Hofman, D.F. Swaab, Eus JW Van Someren, R.M. Buijs, 2006-08-21 The prevalence of obesity in developed countries is fast becoming a health issue on par with infectious diseases and malnutrition Research in this area has grown substantially and includes the neurochemical pathways

of the hypothalamus and its role in regulating energy expenditures in the body This volume in the Progress in Brain Research series examines the emerging role of the hypothalamus as a crucial link between the sensing of nutrients and the control of insulin sensitivity glucose uptake and glucose production the integrative role of the hypothalamus in thyroid and bone metabolism the interaction between circadian information and energy metabolism and the important interplay between the immune system and energy metabolism All contributors are recognized experts in their respective specialities Provides expanded coverage of hypothalamic mechanisms involved in energy metabolism Includes many outstanding full colour illustrations Contains special sections on circadian rhythms immune system thyroid and bone metabolism Cumulated Index Medicus ,1991 *Epigenetics in Health and Disease* ,2023-04-03 Epigenetics in Health and Disease Volume 197 in the Progress in Molecular Biology and Translational Science series highlights new advances in the field with this new volume presenting interesting chapters on An Introduction to epigenetics in health and disease State of the art techniques for epigenetics study Computational biology in epigenetics Artificial intelligence and machine learning in epigenetics CRISPR Cas systems in epigenetics modification for health Mechanisms of DNA methylation and histone modifications Non coding RNA in epigenetics Role of DNA Methylation in cardiovascular diseases Role of epigenetics in renal diseases and much more Additional chapters update on Histone modifications in fat metabolism and obesity Role of DNA methylation in diabetes and obesity Epigenetic regulons in Alzheimer s disease Epigenetics in heredity disease Epigenetics of aging Epigenetics in cancer development diagnosis and therapy Microbiota and epigenetics health impact Epigenetics in Fetal Alcohol Spectrum disorder and much more Provides the authority and expertise of leading contributors from an international board of authors Presents the latest release in the Progress in Molecular Biology and Translational Science series Includes the latest information on Epigenetics in Health and Disease Emery's Elements of Medical Genetics E-Book Peter D Turnpenny,Sian Ellard,2016-11-30 Everything a student needs to know about medical genetics is here in the 15th edition of this award winning textbook Thoroughly updated and revised throughout to map a fast moving area the 15th edition continues Emery s enviable reputation for successfully balancing up to dateness in a rapidly developing field with a strong basis in practical clinical genetics for medical students With MCQs and Case Based Review Questions end of chapter summaries it is the essential tool for this complex but foundational topic for all medical undergraduates as well as postgraduates seeking to improve their understanding and knowledge Divided into three restructured sections to make the book easier to use for a variety of readers Scientific Basis of Human Genetics Genetics in Medicine and Genomic Medicine Clinical Genetics Counselling and Ethics Interactive self assessment questions Case based questions Online hyperlinks to important genetics websites and clinical databases Update of clinical figures to include more full colour images An extensive glossary of terms Full colour art to visualise the appearance of genetic disorders and assist with the understanding of complex genetic structures Explore the social ethical and counselling issues surrounding the study and treatment of genetic disorders

Elements boxes at the end of each chapter summarizing the basics at a glance Biomedical Index to PHS-supported Research ,1989 Annual Review of Eating Disorders Part 2 - 2006 Stephen Wonderlich,James Mitchell,Scott Crow,Liz Boath,Howard Steiger,2005-12 This book contains reviews from leading scientists and clinicians drawing together the latest developments in the ten key topics covering the major areas of eating disorders including bulimia body image socio cultural issues and anorexia This volume compliments Annual Review of Eating Disorders Part 1 Together the two books cover the twenty main topics identified by the Academy of Eating Disorders as providing essential knowledge in the field It is ideal for busy clinicians with a clear emphasis on clinical implications and is supported by the American Academy for Eating Disorders Clinicians and health researchers involved in the area of eating disorders will find this review invaluable as will professional organisations for psychologists psychiatrists dieticians general practitioners paediatricians counsellors and educators

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