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

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Genetic variation in brwon 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; aP2-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 UCP1deficient 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." 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 dietinduced 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 UCPL.

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

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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 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 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 Bibliography of Genetic Variation and Nutrition A. P. Simopoulos, B. Childs, 1990-06-20 Genetic Diagnosis of Agriculture ,1998 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

disorders Elements boxes at the end of each chapter summarizing the basics at a glance **Biomedical Index to** Annual Review of Eating Disorders Part 2 - 2006 Stephen Wonderlich, James PHS-supported Research ,1989 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 Oxford Textbook of Endocrinology and Diabetes John A.H. Wass, Paul M. Stewart, 2011-07-28 Now in its second edition the Oxford Textbook of Endocrinology and Diabetes is a fully comprehensive evidence based and highly valued reference work combining basic science with clinical guidance and providing first rate advice on diagnosis and treatment Endocrine and Metabolic Diseases - Genetic Impact and Therapies Ralf Jockers, Isabelle Jéru, Bruno Michel Fève, 2022-11-22 *An A-Z of Genetic Factors in Autism* Kenneth Aitken, 2011-04-15 This volume explains the biology and genetics of ASD and provides clinicians and researchers with a comprehensive summary of each genetic factor including the research that links it to ASD diagnosis and treatment issues and related animal models as well as detailing relevant professional organisations and avenues for further research Eating Disorders and Obesity, Second Edition Christopher G. Fairburn, Kelly D. Brownell, 2013-12-20 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 Suggestions for further reading at the end of each chapter replace extended references and enhance the practical value and readability of the volume Principles and Concepts of Behavioral Medicine Edwin B. Fisher, Linda D. Cameron, Alan J. Christensen, Ulrike Ehlert, Yan Guo, Brian Oldenburg, Frank J. Snoek, 2018-10-08 Principles and Concepts of Behavioral Medicine A Global Handbook Edwin B Fisher Linda D Cameron Alan J Christensen Ulrike Ehlert Brian Oldenburg Frank J Snoek and Yan Guo This definitive handbook brings together an international array of experts to present the broad cells to society perspectives of behavioral medicine that complement conventional models of health health care and prevention In addition to applications to assessment diagnosis intervention and management contributors offer innovative prevention and health promotion strategies informed by current knowledge of the mechanisms and pathways of behavior change Its range of conceptual and practical topics illustrates the central role of behavior in health at the individual family community and

population levels and its increasing importance to person centered care The broad perspectives on risk e g stress lifestyle management issues e g adherence social support and overarching concerns e g inequities health policy makes this reference uniquely global as it addresses the following core areas The range of relationships and pathways between behavior and health Knowing in behavioral medicine epistemic foundations Key influences on behavior and the relationships among behavior health and illness Approaches to changing behavior related to health Key areas of application in prevention and disease management Interventions to improve quality of life The contexts of behavioral medicine science and practice Principles and Concepts of Behavioral Medicine opens out the contemporary world of behavior and health to enhance the work of behavioral medicine specialists health psychologists public health professionals and policymakers as well as physicians nurses social workers and those in many other fields of health practice around the world **Kumar and Clark's** Clinical Medicine E-Book Parveen Kumar, Michael L Clark, 2012-06-04 Kumar including all the major lesion morphologies covered in a single page 16 new authors New sections on protein synthesis energy production and stem cells New members of the International Advisory Board from India South Africa Poland and the Middle East 7 new online chapters from the International Advisory Board Key online features 30 extra short chapters online written by members of the International Advisory Board to cover key international issues such as malaria envenoming and HIV Animated practical procedures including lumbar puncture central venous and bladder catheterization arterial cannulation etc heart and lung sounds and interactive surface anatomy available online Full text online through StudentConsult Add your own notes and bookmarks Search across all the StudentConsult resources you own online in one place New to this edition New chapter on palliative medicine Five times the number of margin clinical photos New echocardiography images Double the number of dermatological images including all the major lesion morphologies covered in a single page 16 new authors New sections on protein synthesis energy production and stem cells New members of the International Advisory Board from India South Africa Poland and the Middle East 7 new online chapters from the International Advisory Board **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 akabas obesity Genetic Factors in Autism Kenneth J. Aitken, 2010 The book covers the main genetic disorders associated with autism including those linked to growth differences neurodevelopmental problems gastrointestinal disturbances epilepsy and many others It alphabetically lists the conditions next to information about how common they are causes signs symptoms and methods of treatment and management Handbook of Evidence-Based Interventions for Children and Adolescents Lea Theodore, 2016-07-20 A step by step resource for treating more than 40 prevalent issues with proven strategies This comprehensive handbook for evidence based mental health and learning interventions with children and adolescents is distinguished by its explicit yet concise guidance on implementation in practice With a compendium of proven strategies for resolving more than 40 of the most pressing and prevalent issues facing young people the book provides immediate guidance and uniform step by step instructions for resolving issues ranging from psychopathological disorders to academic problems Busy academics practitioners and trainees in schools and outpatient clinical settings will find this resource to be an invaluable desktop reference for facilitating well informed decision making Unlike other volumes that ignore or merely reference the evidence base of various interventions this book focuses on providing immediate empirically supported guidance for putting these strategies into direct practice Issues covered include crisis interventions and response social and emotional issues academic learning issues psychopathological disorders neuropsychological disorders and the behavioral management of childhood health issues Each chapter follows a consistent format including a brief description of the problem and associated characteristics etiology and contributing factors and three evidence based step by step sets of instructions for implementation Additionally each chapter provides several websites offering further information about the topic Featuring contributions from leading scholars and practitioners on each issue covered this book will be a valuable resource for child clinical and school psychologists counselors social workers and therapists as well as other health and mental health professionals whose primary practice is with children and adolescents Key Features Demonstrates step by step evidence based interventions for more than 40 common childhood issues Provides treatment procedures that can be immediately put into practice Covers a wide range of mental health and academic learning issues for children and adolescents Relevance for both school based and clinically based practice Includes contributions by noted experts in the field

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