

The Epigenomic Analysis of Human Obesity

Christopher G. Bell ^{1,2,3,4}

Objective: Analysis of the epigenome—the chemical modifications and packaging of the genome that can influence or indicate its activity—enables molecular insight into cell type-specific machinery. It can, therefore, reveal the pathophysiological mechanisms at work in disease. Detected changes can also represent physiological responses to adverse environmental exposures, thus enabling the epigenetic mark of DNA methylation to act as an epidemiological biomarker, even in surrogate tissue. This makes epigenomic analysis an attractive prospect to further understand the pathobiology and epidemiological aspects of obesity. Furthermore, integrating epigenomic data with known obesity-associated common genetic variation can aid in deciphering their molecular mechanisms.

Methods and Conclusions: This review primarily examines epidemiological or population-based studies of epigenetic modifications in relation to adiposity traits, as opposed to animal or cell models. It discusses recent work exploring the epigenome with respect to human obesity, which to date has predominately consisted of array-based studies of DNA methylation in peripheral blood. It is of note that highly replicated BMI DNA methylation associations are not causal, but strongly driven by coassociations for more precisely measured intertwined outcomes and factors, such as hyperlipidemia, hyperglycemia, and inflammation. Finally, the potential for the future exploration of the epigenome in obesity and related disorders is considered.

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Introduction

Epigenetic factors include the chemical modifications of DNA and the proteins that the DNA wraps around, which influence or may indicate the activity of genes. Deciphering these marks can be a powerful method to understand the specialized functioning of a cell and organs (1). They may also inform how molecular mechanisms are impeded in disease or because of adverse environments.

The dramatic increase of obesity rates clearly points toward nongenetic or environmental factors as the significant driver. Identified genetic susceptibilities are also modulated by these external influences (2,3). This has led to considerable interest in studying the epigenome to potentially quantify gene activity changes due to this environment and to possibly gain molecular understanding of the pathophysiological consequences of the obese state. Crucial biological understanding of obesity and its consequences is still lacking (4,5) and would help focus vital preventive measures to counter obesity's substantial morbidity and mortality risk (6).

The Epigenome

DNA is packaged at the strand level by wrapping around histone proteins composed of eight subunits, two of each of histones 2A, 2B, 3, and 4. The histone proteins possess tails that can be post-translationally modified, including the addition of methyl or acetyl groups to lysine (K) molecules on histone 3 (H3). These additions can be related to active or repressed regions depending on which K is modified. Amino acid deviation in the protein structure of these histone molecules, termed histone variants, also modifies activity and can be associated with disease processes (7).

Chemical modifications of DNA itself include DNA methylation, the most common, stable, and well-studied process, which is the addition of a methyl group onto the 5' carbon of cytosine. This robust chemical mark is due to the strong covalent carbon-to-carbon bond that connects cytosine to the methyl group. In differentiated cells, this occurs in the DNA sequence predominantly within the context of a CpG dinucleotide, which is where guanine follows cytosine in the 5' to 3' direction on one DNA strand. It acts canonically as a repressive mechanism within gene promoters. However, additional DNA

¹ MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK; ² Epigenomic Medicine, Biological Sciences, Faculty of Environmental and Natural Sciences, University of Southampton, Southampton, UK; ³ Human Development and Health Academic Unit, Institute of Developmental Sciences, University of Southampton, Southampton, UK; ⁴ Department of Twin Research and Genetic Epidemiology, King's College London, London, UK. Correspondence: Christopher G. Bell (cgb@mrcc.soton.ac.uk)

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Chapter 14 Epigenomic Factors In Human Obesity

Trygve O. Tollefsbol



Chapter 14 Epigenomic Factors In Human Obesity:

Epigenetics in Human Disease Trygve O. Tollefsbol, 2012-07-26 Epigenetics is one of the fastest growing fields of sciences illuminating studies of human diseases by looking beyond genetic make up and acknowledging that outside factors play a role in gene expression The goal of this volume is to highlight those diseases or conditions for which we have advanced knowledge of epigenetic factors such as cancer autoimmune disorders and aging as well as those that are yielding exciting breakthroughs in epigenetics such as diabetes neurobiological disorders and cardiovascular disease Where applicable attempts are made to not only detail the role of epigenetics in the etiology progression diagnosis and prognosis of these diseases but also novel epigenetic approaches to the treatment of these diseases Chapters are also presented on human imprinting disorders respiratory diseases infectious diseases and gynecological and reproductive diseases Since epigenetics plays a major role in the aging process advances in the epigenetics of aging are highly relevant to many age related human diseases Therefore this volume closes with chapters on aging epigenetics and breakthroughs that have been made to delay the aging process through epigenetic approaches With its translational focus this book will serve as valuable reference for both basic scientists and clinicians alike Comprehensive coverage of fundamental and emergent science and clinical usage Side by side coverage of the basis of epigenetic diseases and their treatments Evaluation of recent epigenetic clinical breakthroughs

Childhood Obesity Michael I. Goran, 2016-10-14 Childhood obesity has reached epidemic proportions in the United States and continues to increase in prevalence in almost all countries in which it has been studied including developed and developing countries around the globe The causes of obesity are complex and multi factorial Childhood obesity becomes a life long problem in most cases and is associated with long term chronic disease risk for a variety of diseases including type 2 diabetes cardiovascular disease non alcoholic fatty liver disease as well as psychosocial issues and obesity seems to affect almost every organ system in the body In recent years there has been tremendous progress in the understanding of this problem and in strategies for prevention and treatment in the pediatric years Childhood Obesity Causes Consequences and Intervention Approaches presents current reviews on the complex problem of obesity from the multi level causes throughout early life before adulthood and the implications for this for long term disease risk It reviews numerous types of strategies that have been used to address this issue from conventional clinical management to global policy strategies attempting to modify the global landscape of food nutrition and physical activity Each chapter is written by a global authority in his or her respective field with a focus on reviewing the current status and recent developments The book features information on contributing factors to obesity including developmental origins social family birth cohort studies influence of ethnicity and global perspectives It takes a life course approach to the subject matter and includes exhaustive treatment of contributing factors to childhood obesity such as assessment environmental factors nutrition and dietary factors host factors interventions and treatment consequences and further action for future prevention This broad

range of topics relevant to the rapidly changing field of childhood obesity is suitable for students health care professionals physicians and researchers

Adipose Tissue and Adipokines in Health and Disease Giamila Fantuzzi, Carol Braunschweig, 2014-04-25 The field of adipose tissue biology has been expanding at a very rapid pace in the last few years Numerous advances have been made since publication of the first edition of this book in terms of basic adipocyte biology understanding of the determinants of obesity distribution of body fat and weight loss as well as the mechanisms linking excess adiposity to various co morbidities Adipose Tissue and Adipokines in Health and Disease Second Edition contains updated chapters from the previous volume but as the field has evolved some areas covered in the first edition have been refocused to address the new knowledge The volume is divided in four sections the first two deal with basic adipose tissue and adipokine biology while the last two address the problem of obesity and alterations in adipose tissue function from an epidemiological and clinical standpoint The chapters are written by experts in their fields and include the most up to date scientific information Adipose Tissue and Adipokines in Health and Disease Second Edition is a useful resource for physicians interested in adipose tissue biology and basic scientists who want to know more about applied aspects of the field The book targets endocrinologists residents and fellows internists nutritionists and general practitioners who are exposed to an ever expanding obese population

Medical Epigenetics, 2021-08-27 Selected for Doody's Core Titles 2024 in Clinical Genetics Medical Epigenetics Second Edition provides a comprehensive analysis of epigenetics in health management across a broad spectrum of disease categories and specialties and with a focus on human systems epigenetic diseases that affect these systems and evolving modes of epigenetic based treatment Here more than 40 leading researchers examine how each human system is affected by epigenetic maladies offering an all in one resource on medical epigenetics not only for those directly involved with health care but investigators in life sciences biotech companies graduate students and others who are interested in applied aspects of epigenetics Incorporating both diagnostic and prognostic epigenetic approaches this volume also fully supports the application of epigenetics in precision medicine This second edition of Medical Epigenetics a volume in the Translational Epigenetics series has been fully revised to address recent advances in disease epigenetics and role of epigenetics in precision medicine with all new chapters on skin cancer epigenetics network analysis in medical epigenetics machine learning in epigenetic diseases and clinical trials of epigenetics drugs Features chapters from leading researchers and clinicians dedicated to the burgeoning role of epigenetics in medical practice Covers emerging topics including twin epigenetics as well as epigenetics of gastrointestinal disease muscle disorders endocrine disorders ocular medicine pediatric diseases sports medicine noncoding RNA therapeutics pain management and regenerative medicine Organized from system disorders to multi system disorders that involve epigenetic aberrations Examines the role of epigenetics in precision medicine

Personalized Epigenetics Trygve Tollefsbol, 2024-07-17 Personalized Epigenetics Second Edition discusses the core translatability of epigenetics to health management of individuals who have unique variations in their epigenetic

signatures that can guide both disorder and disease prevention and therapy Fully updated and revised this new edition details inter individual variability in the major epigenetic process in humans consisting of DNA methylation histone modifications noncoding RNA and the diagnostic prognostic and therapeutic potential of the field It also reviews the impact of the environment on epigenetic variations among individuals and the role of pharmacology and drug development in personalized epigenetics Most importantly the text covers personalized epigenetics from a disease oriented perspective presenting chapters that provide advances in widespread disorders or diseases including diabetes cancer autoimmune disorders obesity cardiovascular diseases neurological disorders and pain management Includes new chapters on topics such as the limitations of personalized epigenetic variation comparisons personalized epigenetics technologies epigenetics of personalized nanomedicine personalized epigenetic management of diabetes epigenetics and chemoresistance and personalized epigenetics and neurological disorders Covers key methodological processes that are important in personalized medicine Offers disease research case studies to provide in depth discussion of examples of recent epigenetic research on a disease area Features topics such as forensic epigenetics epigenetics of personalized toxicity limitations of epigenetic variation comparisons and nanomedicine and nutrigenomics as applied to personalized epigenetics

Epidemiology of Obesity in Children and Adolescents Luis A. Moreno,Iris Pigeot,Wolfgang Ahrens,2011-01-12 Despite adults best preventive efforts childhood obesity is on the rise in most areas of the world and with it the prevalence of Type 2 diabetes hypertension cardiovascular disease and other formerly adult onset conditions Epidemiology of Obesity in Children and Adolescents takes the global ecological approach that is needed to understand the scope of the problem and its multiple causes and mechanisms and to aid in developing more effective prevention and intervention programs In the book s first half experts present a descriptive summary of youth obesity trends in ten world regions broken down by age group gender socioeconomic status and risk factors Complementing these findings part two reviews the evidence base regarding the variables separately and in combination having the most significant impact on young people s development of obesity including Genetic and nutrigenomic factors Environmental and psychosocial factors such as family shopping and eating habits and access to healthful foods Neuroendocrine regulation Prenatal and neonatal factors e g gestational diabetes of the mother Dietary factors from nutrient content to young people s food preferences Physical activity versus sedentary behavior Epidemiology of Obesity in Children and Adolescents is necessary reading for the range of professionals involved in curtailing this epidemic including public health specialists epidemiologists pediatricians nurses nutritionists psychologists health educators and policymakers

Sadikot's International Textbook of Diabetes Kamlakar Tripathi,Banshi Saboo,2019-04-30 This book is a complete guide to the diagnosis and management of diabetes Divided into eight sections the text begins with an overview of the history epidemiology and pathogenesis of the disease The next chapters discuss different types diabetes diagnosis managements techniques and monitoring The following sections cover chronic and acute

complications and diabetes in special situations such as in pregnancy and during Ramadan The book concludes with discussion on transplant gene and stem cell therapy psychosocial aspects and public health and economics The comprehensive text is further enhanced by clinical photographs diagrams and exhaustive references Key points Comprehensive guide to diagnosis and management of diabetes Covers different types of diabetes and potential complications Includes discussion on diabetes in special situations such as in pregnancy or during Ramadan Features clinical photographs diagrams and exhaustive references

Gene Regulation and Epigenetics Carsten Carlberg, 2024-10-04 This book delves into the fascinating realm of eukaryotic gene regulation The specific expression of genes shapes the phenotype of cells and tissues The regulation of gene expression including up and downregulation is a fundamental aspect of nearly all physiological processes both in health and disease These dynamic processes respond to various daily challenges such as dietary changes and infections Therefore it is crucial for not only biologists and biochemists but also all students in biomedical disciplines to understand gene regulation concepts This foundational knowledge will benefit them in their specialized fields A comprehensive understanding of transcription factors and the mechanisms that alter their activity is a fundamental goal of modern life science research Epigenetics refers to the packaging and accessibility of the genome in each of the trillions of cells in our bodies The prefix epi meaning upon above or beyond indicates that epigenetic processes do not alter the DNA sequence of our genome adding a layer of information beyond that encoded in our genome Genomic DNA is wrapped around complexes of histone proteins helping it fit into a cell nucleus with a diameter of less than 10 m This protein DNA complex is known as chromatin The content of this book is linked to the Molecular Medicine and Genetics course which the author has lectured on in various forms since 2002 at the University of Eastern Finland in Kuopio This book is an updated version of the textbooks Mechanisms of Gene Regulation and Human Epigenomics It is divided into 16 chapters Following two introductory chapters four chapters explore gene regulation from the perspective of transcription factors while another four chapters focus on chromatin and non coding RNA Three chapters then discuss the impact of epigenetics from a health perspective and the final three chapters address epigenetics from the perspective of diseases A glossary in the appendix explains the major specialist terms

Textbook of Diabetes Richard I. G. Holt, Allan Flyvbjerg, 2024-01-17 Textbook of Diabetes Classic textbook providing diabetologists and endocrinologists with illustrated and clinically focused content on diabetes Now in its sixth edition the Textbook of Diabetes has established itself as the modern international guide to diabetes Sensibly organized and easy to navigate with exceptional illustrations the textbook hosts an unrivalled blend of clinical and scientific content Written by highly experienced editors and international contributors all of whom have provided insight on new developments in diabetes care These include the most recent guidelines from the European Association for the Study of Diabetes EASD the American Diabetes Association ADA Diabetes UK and the National Institute for Health and Care Excellence NICE and information on the latest treatment modalities used around the world The textbook includes free access

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Drug Discovery in Cancer Epigenetics Gerda Egger, Paola Arimondo, 2015-11-19 Drug Discovery in Cancer Epigenetics is a practical resource for scientists involved in the discovery testing and development of epigenetic cancer drugs Epigenetic modifications can have significant implications for translational science as biomarkers for diagnosis prognosis or therapy prediction Most importantly epigenetic modifications are reversible and epigenetic players are found mutated in different cancers therefore they provide attractive therapeutic targets There has been great interest in developing and testing epigenetic drugs which inhibit DNA methyltransferases histone modifying enzymes or chromatin reader proteins The first few drugs are already FDA approved and have made their way into clinical settings This book provides a comprehensive summary of the epigenetic drugs currently available and aims to increase awareness in this area to foster more rapid translation of epigenetic drugs into the clinic Highlights the potential of epigenetic alterations in cancer for drug development Covers the tools and methods for epigenetic drug discovery preclinical and clinical testing and clinical implications of epigenetic therapy Provides important information regarding putative epigenetic targets epigenetic technologies networks and consortia for epigenetic drug discovery and routes for translation

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