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Vinood B. Patel
Victor R. Preedy
Editors

Handbook of Nutrition, Diet, and Epigenetics

 Springer

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Vinood B. Patel • Victor R. Preedy
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Handbook of Nutrition, Diet, and Epigenetics

With 416 Figures and 143 Tables

 Springer

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Preface

The well-being of humankind is not only dependent upon individuals receiving adequate nutrition but also upon their genetic makeup. Genes may encode proteins responsible for structural components (e.g., membranes, subcellular organelles) and dynamics (e.g., enzymes, receptor–postreceptor cascades). Many of these components will require, from the outset, an adequate diet. For example, some antioxidant enzymes are critically dependent on the diet. This is illustrated by the role of dietary selenium which is necessary for glutathione peroxidase activities, while copper and zinc are necessary for superoxide dismutase activities. However, there is an increasing body of evidence to suggest that nutrition itself may alter the way in which genes are expressed via the process of epigenetics. Definitions of epigenetics vary and include modifications in the functional expression of DNA. This may involve changes in, or the influence of, DNA methylation, noncoding RNA, chromatin, histone acetylation or methylation, genomic imprinting, and other processes. There are many dietary components that impose epigenetic changes including folate, B vitamins, betaine, choline, and other extracts from plants, foods, and beverages. In fact, the knowledge base of how dietary components impact epigenetic processes has increased markedly over the past few years. As a prelude to understanding the role of epigenetics, it is also necessary to understand the basics of cellular and molecular biology, as well as the clinical basis of health and disease. However, marshaling all the information on the complex relationships between cellular and molecular biology, diet and nutrition, health and disease, and epigenetic processes is somewhat difficult due to the myriad of material. To address this, the editors have compiled the *Handbook of Nutrition, Diet, and Epigenetics*.

The book is divided into the following parts:

Part I. Introductory Material and Foundations

Part II. Organs, Disease, and Life Stages

Part III. Influence of Diet and Nutrition on Epigenetics

Part IV. Practical Techniques and Applications

Part I Introductory Material and Foundations covers biology of the cell, overviews, and comparative epigenetics. **Part II Organs, Disease, and Life Stages** covers weight control, metabolic syndrome and obesity, diabetes, insulin and

glucose, the cardiovascular system, the nervous system, cancers and immune function, the intestinal tract, kidney, muscle and bone, life stages, pregnancy, development and programming, transgenerational effects, and aging. **Part III Influence of Diet and Nutrition on Epigenetics** covers energy, general treatments and nutritional modifications, lipids and proteins as macronutrients and their components, vitamins and minerals, combinations (mixtures of components), specific foods and nutraceuticals, and nutritional toxicology and adverse effects. **Part IV Practical Techniques and Applications** covers multilocus methylation assays, beadchips, bioinformatics databases, microRNAs, mass spectrometry, embryonic stem cells, and molecular pathways and resources.

It is difficult to list all the chapters as there are just over 120, and some cover numerous analytical or disease-based domains. The editors recognize the difficulties in assigning chapters to specific parts of the book as some chapters may well be suitable for two or more sections. Nevertheless, there is a wide breadth of material available. There are also unique features in this handbook, whereby each of the chapters includes the following sections:

- Dictionary of Terms
- Key Facts
- Summary Points

These features enable the transdisciplinary and transintellectual divides to be bridged.

Contributors are authors of international and national standing, leaders in the field, and trendsetters. Emerging fields of epigenetics in relation to diet and nutrition are also incorporated in the *Handbook of Nutrition, Diet, and Epigenetics*. This represents essential reading for nutritionists, dietitians, health care professionals, research scientists, molecular and cellular biochemists, physicians, general practitioners, public health practitioners, as well as those interested in health in general.

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Victor R. Preedy

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About the Editors



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Victor R. Preedy (B.Sc., Ph.D., D.Sc., FRSB, FRSPH, FRCPath, FRSC) is a senior member of King's College London, where he is also Director of the Genomics Centre and a member of the Faculty of Life Sciences and Medicine.

Professor Preedy graduated in 1974 with an Honors Degree in Biology and Physiology with Pharmacology. He gained his University of London Ph.D. in 1981. In 1992, he received his Membership of the Royal College of Pathologists, and in 1993 he gained his second doctoral degree for his outstanding contribution to protein metabolism in health and disease. Professor Preedy was elected as Fellow to the Institute of Biology in 1995 and to the Royal College of Pathologists in 2000. Since then, he has been elected as Fellow to the [Royal Society for the Promotion of Health](#) (2004) and the [Royal Institute of Public Health](#) (2004). In 2009, Professor Preedy became Fellow of the Royal Society for Public Health and, in 2012, Fellow of the Royal Society of Chemistry. In his career, Professor Preedy has carried out research at the National Heart Hospital (part of Imperial College London), the School of Pharmacy (now part of University College London), and the MRC Centre at Northwick Park Hospital. He has collaborated with research groups in Finland, Japan, Australia, the USA, and Germany. He is a leading expert in the science of health and has a long-standing interest in food and nutrition for over 30 years, especially related to tissue pathology and cellular and molecular biology. He has lectured nationally and internationally. To his credit, Professor Preedy has published over 600 articles, which include peer-reviewed manuscripts based on original research, abstracts and symposium presentations, reviews, and numerous books and volumes.

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Part I

Introductory Material and Foundations



Environmental Effects on Genomic Imprinting in Development and Disease

1

Rakesh Pathak and Robert Feil

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Abstract

Genomic imprinting mediates the parent-of-origin-specific, mono-allelic expression of many protein-coding genes and noncoding RNAs. This paradigm for epigenetic gene regulation plays diverse roles in mammalian development, growth and behavior. Mechanistically, it involves parentally inherited DNA methylation marks that control clusters of imprinted genes. Perturbation of these epigenetic imprints affects embryonic and postnatal development and leads to complex diseases in humans, including different types of diabetes. This chapter discusses imprinted genes, with emphasis on those that control metabolism and cellular proliferation, several of which encode proteins of the insulin-like growth factor/insulin signaling pathway. Nutrition, chemical pollutants, and other environmental cues can readily perturb DNA methylation imprints, not only during development, but sometimes even in adults. Such epigenetic alterations

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(“epimutations”) may affect imprinted gene expression and, hence, can have deleterious effects on phenotype. In the future, clinical and environmental imprinting studies will gain from taking a broader approach that considers not only the imprinted gene loci themselves, but also similarly controlled loci located elsewhere in the genome.

Keywords

Epigenetics · Environment · Genomic imprinting · DNA methylation · Growth · Metabolism · IGF/Insulin pathway · Endocrine disruptor

List of Abbreviations

ART	Assisted Reproductive Technology
BPA	Bisphenol A
BWS	Beckwith-Wiedemann Syndrome
ICR	Imprinting control region
IGF	Insulin-like growth factor
INS	Insulin
IUGR	Intra-uterine growth restriction
ncRNA	Noncoding RNA
SRS	Silver Russell Syndrome
TNDM	Transient neonatal diabetes mellitus

Introduction

Epigenetic mechanisms contribute to the establishment and maintenance of stable patterns of gene expression during development and throughout postnatal life. DNA methylation at cytosine residues is the best studied epigenetic modifications in mammals. It plays essential roles in cells and tissues. These include stable repression of endogenous retroviruses and the tissue-specific silencing of developmental genes, particularly germ line genes, which become silenced in the embryo. DNA methylation also contributes to X-chromosome inactivation. This is a gene dosage mechanism in female embryos that leads to the repression of most genes on one of the two X chromosomes.

The current chapter focuses on another gene dosage mechanism for which cytosine methylation is essential, namely genomic imprinting (Bartolomei and Ferguson-Smith 2011). It introduces the roles of imprinted gene expression in mammalian development and its perturbation in disease and makes the link with the insulin/IGF signaling pathway, metabolism and growth control. The chapter also discusses how diet and environmental cues may perturb the epigenetic regulation of imprinted genes and that this can have long-lasting phenotypic consequences (Feil and Fraga 2012).

Mammalian genomic imprinting evolved coincident with the emergence of viviparity and the growing importance of placentation and the evolution of defense mechanisms against transposable elements. The oldest imprinted genes arose about 170 million years ago, during the Jurassic period. Today, more than 100 protein-