Preface

Epigenetics, Energy Balance, and Cancer: Impact of Environmentally Induced Genetic Change Without Changing the Genome

Mechanistic studies of energy balance and cancer have largely focused on regulatory effects at the level of metabolic, inflammatory, and endocrine signaling cascades and growth factors, all of which are influenced by genetic interactions with the environment. While genetic effects are hereditary and are primarily determined by the base pair sequence of DNA, recent studies indicate that major effects can be determined also by epigenetic factors that modify gene expression without altering DNA base pair sequence. Thus cancer results from aberrations that occur in oncogene activation and/or tumor suppressor gene inactivation, processes frequently shown to be due to genetic alterations in DNA base pair sequence. These sequence alterations in the genome may exist in the germline where they can be associated with hereditary cancers or they may commonly arise in somatic cells due to gene mutations and/or rearrangements where they are associated with sporadic cancers. In addition to modifications in DNA base pair sequences, genetic readout, resulting in neoplasia, may result from a series of biochemical and structural modifications of DNA and/or its surrounding chromatin proteins to activate or silence oncogene or tumor suppressors resulting in drastic changes in cell biochemistry and growth control. These processes by which the genetic readout is altered by chemical modification of DNA and/or chromatin, without changing DNA sequence, are designated as epigenetics. These changes predominantly include methylation of DNA bases, post-translational modification of chromatin proteins, and synthesis of noncoding RNA capable of altering chromatin tertiary structure and function, as well as stability of gene transcripts. Posttranslational modifications of histones and other chromatin proteins include multiple processes such as methylation, acetylation, phosphorylation, ubiquitination, ADP ribosylation, and many others controlled by a myriad of different enzymes that attach to, respond to, or remove these groups. These
so-called writers, readers, and erasers can be impacted by environmental factors including dietary composition and quantity, physical activity, and others to drastically impact genetic readout.

Although these epigenetic modifications do not alter DNA sequence, their resultant phenotypes are heritable through multiple generations of cell division and may become transgenerational, passing from parent to offspring. Moreover, epigenetic changes in DNA and chromatin can be induced by a variety of exogenous chemical agents including toxins and xenobiotics and by endogenous processes such as inflammation and generation of free radicals. In addition, it is now becoming increasingly clear that biobehavioral phenomenon related to energy balance such as obesity, exercise, caloric restriction, and stress may all change DNA epigenetic marks and may, in fact, affect incidence and pathology of chronic conditions like obesity, diabetes, and cancer. At the same time, epigenetic changes and processes may provide novel targets for precision medicine interventions to prevent or disrupt the linkage between obesity and cancer.

This volume of Epigenetics, Energy Balance, and Cancer will connect the exciting state-of-the-art research activities in epigenetics and energy balance as they both relate to cancer. The reader will obtain a clear understanding of the multiple processes involved in epigenetic modification of DNA and chromatin, which aspects of energy balance induce these changes, how they affect chronic diseases such as obesity and diabetes, and how these changes impact cancer in general and in specific organ systems. The reader will be introduced also to consideration of how epigenetic changes may impact cancer prevention and control and how they may serve as therapeutic targets.

As in the past, we are fortunate to have chapters contributed by leading authorities from around the world for this volume on Epigenetics, Energy Balance, and Cancer. We extend our sincere thanks to all for their efforts and contributions in preparing this volume. In Chap. 1, Andrew D. Kelly and Jean-Pierre J. Issa (Fels Institute for Cancer Research and Molecular Biology, Lewis Katz School of Medicine at Temple University) describe the multiple mechanisms of epigenetic modification and how they relate to cancer. Chapter 2, written by James J. Morrow and Peter C. Scacheri (Case Western Reserve University), describes the higher-order impact of gene enhancer arrangements in chromatin and how enhancer dysfunction may contribute to cancer. Chapters 3–7 then describe how different environmental processes impact the epigenome to contribute to cancer. Thus Chap. 3, written by Francine H. Einstein (Albert Einstein College of Medicine), describes early life epigenetic effects on obesity, diabetes, and cancer. Chapter 4, written by Eswar Shankar and Sanjay Gupta (Case Western Reserve University), focuses on how nutrition and lifestyle factors impact epigenetics of cancer, and in Chap. 5, David A. Skaar, Randy L. Jirtle, and Catherine Hoyo (North Carolina State University) describe environmentally induced alterations in the epigenome and how they may affect obesity and especially cancer in minority populations. In Chap. 6, Giuseppe Lippy (Universitaria di Parma, Italy), Elisa Danese (University of Verona, Italy), and Fabian Sanchis-Gomar (Research Institute of Hospital 12 de Octubre (“i+12”), Madrid Spain) review effects of stress and exercise on epigenetics and
cancer. The impact of gut microbiota on cancer is a relatively new and rapidly growing research area whose epigenetic effects are described in Chap. 7 written by Joice Kuroiwa-Trzmielina (Garvan Institute of Medical Research) and Luke B. Hesson (Lowy Cancer Research Centre and Prince of Wales Clinical School, Sydney Australia). The concluding Chaps. 8–11 describe the epigenetic impact of energy balance on cancer in specific organ systems. In Chap. 8, Andrew M. Kaz (VA Puget Sound Health Care System) and William M. Grady (Fred Hutchinson Cancer Research Center) discuss epigenetics in obesity and esophageal cancer. In Chapter 9, Ruifang Li and Paul A. Wade (National Institute of Environmental Health Sciences) discuss epigenetics in obesity and colon cancer. In Chap. 10, David Heber, Susanne M. Henning, and Zhaoping Li (David Geffen School of Medicine, University of California Los Angeles) describe epigenetic effects of energy balance on prostate cancer, and in Chap. 11, Herbert Yu (University of Hawaii Cancer Center) and Melinda L. Irwin (Yale School of Public Health) discuss how physical activity may influence breast cancer through epigenetic mechanisms.

Overall this volume on Epigenetics, Energy Balance, and Cancer provides a state-of-the-art and transdisciplinary description of the rapidly evolving field of epigenetics and its potential role in mediating the impact of energy balance on cancer. It should serve as an important resource for students at all levels and for practitioners in related fields seeking to better understand this important area of evolving science. It should likewise provide important background information for development of research strategies to further interrogate, promote, and/or interrupt these epigenetic regulatory processes as well as new targets for precision medicine.

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