

Preface: What's Old Is New Again and Now It's Red Hot

As the worldwide obesity pandemic expands, obesity has been associated with an increased risk of more and more cancer types. The original malignancies shown to be associated with obesity included esophageal adenocarcinoma, colon cancer, renal cell cancer, postmenopausal breast cancer, endometrial cancer, and advanced prostate cancer. More recently, obesity has been identified as a risk factor for cancers of the pancreas, gall bladder, and ovary and several hematologic malignancies including leukemia, lymphomas, and myeloma, and the list continues to grow.

From a historical viewpoint, while early studies considered the possibility that inflammation initiated the process of carcinogenesis, this was generally considered to be a local effect associated with tissue injury or chronic infection. With elucidation of DNA structure and function and development of the concept of chemical carcinogens as mutagens, attention turned to identification of activated oncogenes and deactivated tumor suppressor genes in the carcinogenic process. Separate studies demonstrated that inflammation extended beyond the local site, mediated by cellular and humoral components. As noted above, independent epidemiologic studies confirmed an association of obesity with cancer incidence, morbidity, and mortality. Studies to identify the mediators of these processes focused on the effects of obesity on growth factors and hormones and the mechanisms of carcinogenesis they commonly affect. More recently, it has become apparent that adipose tissue, in addition to serving as a fat storage depot, is an intensely active metabolic organ. In obesity, low-grade chronic adipose tissue inflammation occurs, resulting in multiple cellular and humoral inflammatory factors. Seminal studies showing that systemic metabolic disorders, such as insulin resistance, could be mediated, in part, by inflammatory cytokines, synthesized and secreted by adipose tissue, resulted in a whole new approach to understanding and attempting to control obesity-associated comorbidities. Moreover, elucidation of the prostaglandin pathway and its role in inflammation, as well as the observations that anti-inflammatory agents, especially the nonsteroidal anti-inflammatory drugs (NSAIDs), could prevent the development and progression of several forms of neoplasia, provided a major stimulus to the field. A major goal of ongoing research is to inhibit inflammation as an approach to cancer prevention and control.

The above brief description traces the complex transdisciplinary evolution of this area of research endeavor. Not only does it illustrate the impact of sometimes divergent disciplines on the evolution of a concept, but it also indicates the potential value of moving forward in this field with a transdisciplinary approach. Accordingly, the goal of this volume of *Energy Balance and Cancer*, volume 7 in the series, is to highlight the cutting-edge transdisciplinary science linking obesity, inflammation, and cancer. We are grateful to all the authors listed below for their contributions to this volume and look forward to their collective impact in further advancing this rapidly developing field.

This volume first provides information on inflammation as an important link between obesity and insulin resistance, which is in itself linked to promotion of cancer through hyperinsulinemia. The volume then covers some of the most important mechanisms by which obesity leads to inflammation, including the novel inflammasome concept, alterations in chromatin structure, circulating inflammatory factors, unique cellular interactions between adipocytes and macrophages, and the direct link of dietary fat to inflammation and cancer. Subsequently addressed in this volume are a number of target organs and interventional strategies for disrupting inflammation and their effects on cancer prevention and control.

In Chap. 1, Lesley G. Ellies, Andrew Johnson, and Jerrold M. Olefsky (University of California, San Diego) describe the mechanisms by which obesity stimulates low-grade inflammation leading to insulin resistance. Chapter 2, written by Tuo Deng, Christopher J. Lyon, Nan Zhang, Helen Y. Wang, Rong-fu Wang, and Willa A. Hsueh (Weill Cornell Medical College) and Jun Cui (Sun Yat-sen University), reviews the basis for understanding the emerging concept of the inflammasome and its mechanisms of activation and role in obesity. Gerald V. Denis and Deborah J. Bowen (Boston University School of Public Health) describe in Chap. 3 chromatin-based, transcription co-regulatory mechanisms that may link obesity, inflammation, and cancer. Carey Nien-Kai Lumeng (University of Michigan Medical School), in Chap. 4, describes the important role that adipose tissue macrophages play in breast and ovarian cancer. In Chap. 5, Stephanie K. Doerner and Nathan A. Berger (Case Western Reserve University School of Medicine) discuss the impact of different dietary fatty acids on promoting or suppressing colorectal cancer. In Chap. 6, Anamay Sharma, Ahmed Elebiary, Sonia Chowdhury, and Navtej Buttar (Mayo Clinic) describe the contribution of gastric reflux to inflammation in Barrett's esophagus and esophageal adenocarcinoma and potential interventions. In Chap. 7, Stephanie K. Doerner (Case Western Reserve University School of Medicine) and Jason D. Heaney (Baylor College of Medicine) describe the role of obesity-induced intestinal inflammation on colorectal cancer incidence. In Chap. 8, Neil M. Iyengar, Patrick G. Morris and Clifford A. Hudis (Memorial Sloan-Kettering Cancer Center) and Andrew J. Dannenberg (Weill Cornell Medical College) review the emerging evidence supporting the contribution of adipose tissue and chronic breast inflammation to the development of breast cancer. In Chap. 9, the relation of obesity, inflammation, and hepatocellular cancer is discussed by Naim Alkhouri and Arthur McCullough (Cleveland Clinic Lerner College of Medicine at Case Western Reserve University), and in Chap. 10, Jorge Blando, Achinto Saha, Kaoru Kiguchi, and John

DiGiovanni (University of Texas at Austin) describes the role of obesity and inflammation in prostate cancer. Louise R. Howe (Weill Cornell Medical College), in Chap. 11, describes the central role of cyclooxygenase-derived prostaglandins as potential mediators of obesity-related cancer and outlines how targeting this pathway may be protective against obesity-associated carcinogenesis. In Chap. 12, Harmony F. Turk, Jennifer M. Monk, Tim Y. Hou, and Robert S. Chapkin (Texas A&M University) discuss mechanisms through which n-3 polyunsaturated fatty acids interfere with the inflammatory process to suppress carcinogenesis, and in Chap. 13, Gary Stoner and Li-Shu Wang (Medical College of Wisconsin) describe key mechanisms by which naturally occurring dietary compounds reduce the harmful effects of inflammation and the risk for cancer development. In Chap. 14, Stephen D. Hursting, Nikki A. Ford, Sarah M. Dunlap, and Laura M. Lashinger (University of Texas at Austin) and Marcie J. Hursting (Clinical Science Consulting) describe the modification of inflammatory pathways and their impact on cancer by diet and caloric restriction. Ahmad Salameh and Mikhail G. Kolonin, in Chap. 15, describe an innovative approach to adipose tissue control by vascular targeting. In Chap. 16, Michael Gleeson (Loughborough University) describes the anti-inflammatory effects of exercise.

Overall, this volume on Obesity, Inflammation, and Cancer provides an up-to-date status report on the latest developments and state-of-the-art understanding of the role of inflammation in mediating the effects of obesity on cancer and describes possible strategies for targeting inflammation as an approach to cancer prevention and control. The book should be useful for students, researchers, and clinicians, especially those interested in the role of inflammation and its impact on cancer. It is our expectation that this volume will both stimulate research on the role of inflammation in cancer etiology and progression and lead to new approaches and clinical trials for cancer prevention and control by targeting obesity-related inflammation.

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