Energy Balance and Cancer

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Insulin Resistance and Cancer

Epidemiology, Cellular and Molecular Mechanisms and Clinical Implications

Springer

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Preface

The recent and rapid "Westernization" of developing nations characterized by movement from rural to urban environments, growth of manufacturing industries and increased use of motorized transport, have resulted in better education and job opportunities, and increased average income that has clearly been welcomed as an improved quality of life. At the same time, these changes have been accompanied by a significant decrease in physical activity, a departure from traditional diets to consumption of "fast," prepared, high-fat and calorie-dense foods and, as a consequence, increased rates of obesity. The global obesity epidemic has been well-documented in the medical and lay press. It has also been established that obesity is the leading cause of insulin resistance and the accompanying "metabolic syndrome" associated with elevated levels of circulating insulin, and frequently, glucose intolerance, hypertension, and dyslipidemia. Indeed obesity and insulin resistance are the leading risk factors for the development of type 2 diabetes mellitus, also rapidly increasing worldwide.

A more recent discovery, now receiving increasing attention, is that obesity and these same metabolic perturbations are associated with an increased incidence of several forms of cancer. The precise causes or mechanistic links which explain this association are not completely clear. There may be one critical element, but there are data which suggest that multiple different factors contribute.

This book reviews the epidemiological associations between insulin resistance and cancer. This is followed by reviews of animal models which support this relationship and provide insight into potential mechanisms. Several chapters then provide detailed examination of the metabolic, cellular and molecular changes characterizing the insulin resistant state, such as hyperinsulinemia, abnormal metabolism and hormone signaling, and how these interact with various tumor characteristics. For example, some tumors present increased quantities of the fetal form of the insulin receptor, unique regulation of oxidative (Krebs' cycle) metabolism (Warburg effect), as well as mutations in various relevant signaling pathways. Finally, the clinical implications of these data are integrated with considerations of insulin "sensitization" and potential metabolic interventions to prevent and treat cancer. It should be noted that while a number of cancers are associated with obesity, the authors here have focused primarily on breast cancer as a key and significant model.

As this book is designed for a broad audience, early chapters provide reviews of metabolic homeostasis and the molecular details of insulin signaling to provide a framework and understanding for the nonexpert of the concepts and data presented in the later chapters.

On behalf of all the authors, I would like to thank the staff at Springer for their advice and support throughout the preparation of this issue and we sincerely hope you find it a valuable reference and enjoyable to read.

Toronto, ON I. George Fantus, M.D., F.R.C.P.(C)

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