With very few exceptions, eukaryotic cells possess two interdependent genomes, chromosomal and extra-chromosomal. Over the past several decades, cancer research has focused primarily on deciphering the intricate alterations in the chromosomal genome, with until recently, very little attention to its cytoplasmic counterpart. In spite of the enormous complexity of the nuclear genome, which we now fully appreciate after completion of the human genome project, the efforts of cancer researchers are commendable in terms of the tremendous gains made in unraveling the numerous genetic changes in cancer. These changes include discoveries of tumor suppressor genes, oncogenes, and caretaker genes that are often mutated in cancer. Recent studies of genomic profiles are uncovering even more altered and mutated genes in cancer. Besides these findings, several therapeutic targets for chemotherapy are currently made from studies of altered nuclear genetic pathways. Inspite of all these positive efforts, the war on cancer, declared in 1971 by Richard Nixon, is far from being won. Indeed, the failure of chemotherapy is obvious to clinicians, oncologists, and their patients alike. Moreover, the global incidence and prevalence of cancer continue to rise. What are we missing? Which direction should we be taking? Of course, modern integrated nuclear genomics, proteomics, and metabolomics should provide important clues to carcinogenesis, but the contribution of cytoplasmic genetic alterations to carcinogenesis cannot be neglected.

There is extensive bidirectional trafficking and cross talk between the two eukaryotic cell genomes, and these pathways are exploited by the altered cancer cell genetics to its advantage. Thus, targeting just one component of the intricate changes seems insufficient in defeating the cancer cell, because it will quickly adapt using the other genome to sustain its existence. Ignorance of the role of mitochondria in cancer had been a huge oversight and I am pleased that this era is quickly coming to an end. Indeed, Otto Warburg recognized cancer several decades ago as a mitochondrial genetic disease. Since his initial hypothesis says that the genesis of cancer is the damage to the respiration inside the cell, recent evidence conclusively suggests that mitochondrial genetic damage indeed underlies the carcinogenic process.
As a medical student in the late 1980s and early 1990s, all the knowledge we acquired about the mitochondrion was nothing beyond its essential roles in energy production, metabolism of food substrates and inborn errors of metabolism and the diseases they caused. The mitochondrial genome and human diseases were never mentioned in medicine and oncology lectures. This was not accidental and therefore not surprising because the mitochondrial genome had just been published at about that era (1981), and mitochondrial mutagenesis in aging was provided in 1984, with the involvement of mitochondrial genetic alteration in human neurodegenerative disease being published in 1988. Following these discoveries, our knowledge on mitochondrial cytopathies has expanded considerably. Mitochondrial genetics in diseases such as progressive external ophthalmoplegia (PEO), Pearson syndrome (PS) and Kearns-Sayre syndrome (KSS), mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS), myoclonic epilepsy with ragged red fibers (MERRF), Leber’s hereditary optic neuropathy (LHON), and neuropathy, ataxia, and retinitis pigmentosa (NARP) syndromes are well established and form part of clinical diagnostic algorithms in pediatrics and neurology (see Mitochondrial Medicine by DiMauro, Hirano and Schon). However, mitochondrial genome changes in cancer have lagged behind this progress in mitochondria and human diseases simply because mitochondrial mutations associated with cancer were only available in the late 1990s and the plethora of data on mitochondrial genetic alterations and possible causation of cancer is now just appearing at an exponential rate.

A rekindled scientific effort in the fight against cancer is required that integrates the genetics of both genomes. Not only will this renewed direction open up avenues to attack the cancer cell, but it also holds tremendous opportunity for us to appreciate the complexity of this disease. “Mitochondrial Genetics and Cancer” aims at making available in a composite form the genetic alterations of mitochondria to carcinogenesis, especially the contributions of this genome to cancer development and progression. The clinical importance and utility of these genetic alterations are not overlooked. It is my hope that cancer researchers, oncologists, clinicians, medical students, researchers in the pharmaceutical industry, and all interested in the fight against cancer will find this book useful and interesting. It is also my hope that this book will awaken our thinking about cancer research and therapy and stimulate young scientists into considering research in this exciting area. Mitochondria and Cancer (by Singh and Costello) is a complementary book to Mitochondrial Genetics and Cancer, and the reader is encouraged to consult the previous book as well, for some in-depth synthesis of mitochondrial metabolic alterations in cancer.

The chapters in this book are divided into three parts for convenient reference. Part 1 addresses general concepts including mitochondrial genetics, bioenergetics, metabolism, and control of apoptosis. It also examines three levels of communication between the mitochondria and nuclear genomes including tricarboxylic acid cycle enzyme mutations and cancer, nuclear-mitochondrial stress signaling in cancer, and the carcinogenic potential of nuclear integration of mitochondrial DNA fragments. Part 2 deals with mitochondrial genome alterations in cancer, including the contribution of these genetic changes to carcinogenesis. Part 3 focuses...
on the clinical utility of mtDNA changes, with emphasis on mitochondrial genome changes in clinical specimens, early detection of cancer using mitochondrial genome changes, methodologies and methodological issues of measuring mtDNA changes, and finally the strategies and agents explored for targeting mitochondria to treat cancer.

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