

Preface

Chronic lymphocytic leukemia (CLL) is the most common leukemia in the Western world but is rare in Asia. CLL has a highly varied clinical course. While advances in CLL therapy are noted, many patients still succumb to this illness. To date, most CLL patients are diagnosed in early stages and are not in need of immediate therapeutic interventions. These patients are, however, in need of careful counseling and guidance. Once therapy is medically indicated, CLL patients begin a phase of their illness marked by periods of remission, interrupted by relapses and medical complications. Most patients with CLL that are young and in need of therapy will, ultimately, die of their illness. While improvements in CLL therapy over the last 2 decades have resulted in many patients with CLL living active lives, many of these patients are, nevertheless, in need of ongoing psychological and medical attention and intervention: a situation that is likely to intensify with the advent of multiple novel therapies that appear to be of substantial clinical activity in CLL.

Like most progress in medicine, solid advances in the diagnosis, prognosis, and treatment of CLL are rooted in an in-depth understanding of the basic and translational biology of CLL. Major biological principles that underlie and contribute to CLL pathogenesis relate to (1) the invariant but infrequent (1 %/year) descendance of CLL from CD5+ monoclonal B-cell lymphocytosis (MBL); (2) molecular aberrations that contribute to the substantial inter-patient variability in clinical aggressiveness and aggressiveness of CLL; (3) characteristic recurrent CLL cell-intrinsic abnormalities, including acquired genomic copy number aberrations, gene mutations, transcriptome deregulations and epigenetic deregulations; (4) the important role of anti-apoptotic proteins in CLL biology; (5) the central role of the B-cell antigen receptor in CLL pathogenesis; (6) the important contribution of CLL cell-to-cytokine and CLL cell-to-cell interactions collectively referred to as the microenvironment; (7) the acquisition of CLL therapy resistance and the ultimate progression to drug resistant CLL; and (8) CLL-associated immune system deregulations resulting in substantial morbidity including infection proneness and autoimmune cytopenias.

In this book, CLL experts have contributed state-of-the-art summaries of various important aspects of CLL biology and have discussed the translational implication of such findings. This book, which is directed at physicians and researchers alike, aims to educate broadly and deeply. Intentionally, the many aspects and nuances of CLL clinical care that can only really be appreciated through direct patient care are not covered here, but instead, basic aspects of CLL are presented that underlie many of the contemporary decisions that are made in CLL research and clinical settings.

Individual and comprehensive chapters in this book will collectively describe (1) inherited susceptibility of CLL; (2) the B-cell antigen receptor and the role of antigens in CLL; (3) the CLL microenvironment; (4) the anatomy and clinical relevance of recurrent acquired copy number aberrations and gene mutations, including mutations in *TP53*, in CLL; (5) the current understanding of epigenetic deregulation in CLL and the important role of microRNAs in CLL pathogenesis; (6) apoptosis deregulation in CLL; (7) our improving knowledge of Richter's transformation of CLL; (8) critical signal transduction pathways in CLL that may offer novel therapeutic opportunities; (9) molecular CLL biomarkers and information regarding their judicious use; and (10) selected, very exciting novel, but still experimental, therapeutic approaches to CLL.

In summary, we hope that this book will critically inform the community and stimulate interest in CLL, which will ultimately translate into better CLL research, prognostication, and therapy, with the end goal of providing a better outlook for patients afflicted with this common leukemia.

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