

CONTENTS

<b>Foreword</b>	<b>xiii</b>
Nicholas J. Petrelli	

<b>Preface</b>	<b>xv</b>
Benjamin D. Li	

<b>Erratum</b>	<b>xvii</b>
----------------	-------------

<b>Genomics and Proteomics in Predicting Cancer Outcomes</b>	<b>257</b>
Alexander A. Parikh, J. Chad Johnson, and Nipun B. Merchant	

Sequencing of the human genome and the acquisition of genomic data combined with advances in genomic and proteomic technologies have fueled a revolution in understanding disease. The combination of genomics and proteomics has provided a unique opportunity to diagnose, classify, and detect malignant disease, to better understand and define the behavior of specific tumors, and to provide direct and targeted therapy. Nevertheless, challenges remain, including integration and standardization of techniques and validation against accepted clinical and pathologic parameters. This article provides a summary of technologies, potential clinical applications, and challenges.

<b>Targeted Therapy for Solid Tumors: Current Status</b>	<b>279</b>
Amer H. Zureikat and Mark D. McKee	

Targeted cancer chemotherapy agents interfere with receptor tyrosine kinase signaling pathways that promote tumor cell growth. Targeted agents inhibit receptor tyrosine kinase signaling by binding the extracellular component of a growth receptor, binding the soluble ligand that triggers the receptor, or binding intracellular sites that interfere with downstream signaling events.

Since their introduction, targeted agents have proved effective for the treatment of locally advanced, metastatic, and micrometastatic solid tumors. In this article, the targeted agents used for solid malignancies and the evidence for current tumor-specific therapies are reviewed.

**Molecular Pathology—Translating Research into Clinical Practice: An Expanding Frontier in Surgical Oncology**

303

Mary Lowery Nordberg

Molecular assays have now become essential to the pathologist and clinician alike in diagnosing and managing disease. This article highlights the techniques and molecular targets no longer ancillary to basic research. Ripe for discussion are the likely future impact of genetics on clinical care, the potential models for service provision, and the broader ethical, legal, and social issues related to the use of genetic information for nonmedical purposes. Molecular methods are forecasted to increase in assisting in the diagnosis of human diseases. The author's mission is to embrace this discipline and use these technologies in clinical practice.

**Translational Research in Gastric Malignancy**

323

Sara M. Johnson and B. Mark Evers

This article discusses recent advances in gastric cancer research that have improved treatment and outcomes of gastric malignancy, or have the potential to do so. The significance of *Helicobacter pylori* infection and eradication, immunology, host genetics, proto-oncogenes, and epigenetic alterations in gastric cancer are discussed. Abnormal signaling through growth factor pathways (tyrosine kinases and gastrointestinal peptides) presents ample opportunities for therapeutic intervention that are currently being tested in clinical trials. Drugs targeting abnormal epigenetic changes, such as DNA hypermethylation and histone deacetylation, are also on the horizon, although most of this research is still in the preclinical phase. The potential prognostic implications of genetics and immunology in gastric cancer prognosis are also reviewed.

**The Implications of Colorectal Cancer Molecular Biology in Clinical Practice**

341

Hamed Kargozaran, Morton Kahlenberg, and Vijay P. Khatri

Colorectal cancer (CRC) is the third most common malignancy in the United States. Advances in molecular biology have enhanced the understanding of colorectal carcinogenesis. Approximately 75% of CRCs are sporadic; the rest are hereditary or belong to a familial

syndrome. Identification of familial forms of CRC have enabled the development of several models of carcinogenesis and made CRC a well-studied malignancy in terms of molecular pathogenesis. Pathways containing multiple mutations and genetic alterations that play a role in hereditary CRC pathogenesis have been elucidated. Many of the molecular changes seen in these pathways also are involved in the development of sporadic cancers.

**Translation of Recent Advances and Discoveries in Molecular Biology and Immunology in the Diagnosis and Treatment of Pancreatic Cancer**

357

Daniel Albo, Buckminster Farrow, and David H. Berger

Recent advances in understanding the molecular mechanisms of cancer progression have allowed for targeted approaches to the diagnosis and treatment of pancreatic cancer. New biologic markers are emerging that may improve the ability to detect these tumors earlier. Targeted biologic cancer therapies promise more effective and less toxic systemic treatment options. Although a clear “magic bullet” has yet to emerge, this type of targeted approach offers hope in the management of this dreadful disease. This article offers an update on these promising diagnostic and treatment modalities.

**Advances in Experimental and Translational Research in the Treatment of Hepatocellular Carcinoma**

377

Travis Kidner, Menghua Dai, Prasad S. Adusumilli, and Yuman Fong

Hepatocellular cancer (HCC) is the fifth-leading cause of cancer and the third-leading cause of cancer related deaths world-wide. Current treatment options are limited, as HCC has been shown to be a highly resistant type of cancer to most current treatment modalities. Novel approaches are being explored in the fields of gene therapy, viral oncolytics, radioembolization, and several new biologic therapies. This article summarizes these recent clinical findings and discusses what role they will have in the future treatment of HCC.

**Translational Research in Melanoma**

391

Susan Tsai and Michael S. Sabel

Current treatment of malignant melanoma exemplifies not only the need for translational research but also many of the challenges of moving from bench to bedside. Melanoma remains unique among solid tumors in that its treatment primarily is surgical. Radiation is

of limited benefit, and chemotherapy has been disappointing in both the adjuvant and metastatic settings. This leaves clinicians with few options for reducing the chance of recurrence after surgery and for treating unresectable disease. With this in mind, there has been a fervent attempt to identify novel approaches to melanoma therapy and translate them into clinical use.

### **Translational Research in Breast Cancer**

**421**

Quyen D. Chu, Neal Holm, Kerry Byrnes, and Benjamin D. Li

The discovery of 25,000 human genes from the Human Genome Project has had a dramatic impact on the translational landscape of human diseases. Nowhere is the impact more apparent than in the field of cancer, specifically breast cancer. Understanding of the malignant process at a molecular level, coupled with the discovery of novel molecular techniques, has shifted the paradigm of treating breast cancer from a clinical, population-based risk assessment model to one based on molecular classification of disease.

### **Multiple Endocrine Neoplasia**

**439**

Matthew L. White and Gerard M. Doherty

MEN1 and MEN2 are autosomal dominant cancer syndromes with the potential for considerable morbidity and mortality. Better understanding of the molecular pathogenesis in MEN1 and MEN2 has fostered the development of specific DNA screening. Knowing the genetic status of patients is valuable for making decisions regarding surveillance and interventions, such as prophylactic thyroidectomy for medullary thyroid cancer. Identifying new RET pathways has provided molecular targets for therapies that currently are being tested in clinical trials for locally advanced, metastatic, and recurrent medullary thyroid cancer.

### **Index**

**461**