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COPD Cystic Fibrosis Genome heterogeneity-based personalized prevention Personalized Treatment Options in Dermatology Hepatitis B Virus Heterogeneity Economic Dimensions of Personalized and Precision Medicine Personalized Pricing with Heterogeneous Mismatch Costs The Heterogeneity of Cancer Metabolism The Heterogeneity of Cancer Metabolism Deciphering Invasive Breast Cancer Heterogeneity for Personalised Therapy Oncology in the Precision Medicine Era Exploring Tumor Heterogeneity Cancer Genomics The Impact of Inter- and Intra-tumoral Heterogeneity on the Treatment of Cancer Developing a Protocol for Observational Comparative Effectiveness Research: A User's Guide Applications of Intertumoural, Intratumoural and Intermolecular Heterogeneity for Personalised Medicine in Colorectal Cancer Severe Asthma Hepatocellular Carcinoma Spectrums of Amyotrophic Lateral Sclerosis Year Book of Pathology and Laboratory Medicine 2013, Personalized Management of Gastric Cancer Leveraging Heterogeneous Information Networks for Personalized Entity Recommendation Effect of Braf V600E Heterogeneity on Melanoma Pathogenesis Heterogeneity in Asthma Progress and Challenges in Precision Medicine Economic Dimensions of Personalized and Precision Medicine Computational Methods for Precision Oncology Measuring the Potential Health Impact of Personalized Medicine Experimental Methods in Survey Research Metastatic Progression and Tumour Heterogeneity Taxonomy Matching Using Background Knowledge Behavioural Public Policy Statistical Methods for Learning Patients Heterogeneity and Treatment Effects to Achieve Precision Medicine Personalized Psychiatry Tumor Liquid Biopsies Combating Tumor Heterogeneity with Early Cancer Detection and Immunotherapy Personalized Medicine in the Making Introduction to Meta-Analysis Hypoxia and Human Diseases PET-Based Molecular Imaging in Evolving Personalized Management Design, An Issue of PET Clinics, E-Book

Personalized Psychiatry presents the first book to explore this novel field of biological psychiatry that covers both basic science research and its translational applications. The book conceptualizes personalized psychiatry and provides state-of-the-art knowledge on biological and neuroscience methodologies, all while integrating clinical phenomenology relevant to personalized psychiatry and discussing important principles and potential models. It is essential reading for advanced students and neuroscience and psychiatry researchers who are investigating the prevention and treatment of mental disorders. Combines neurobiology with basic science methodologies in genomics, epigenomics and transcriptomics Demonstrates how the statistical modeling of interacting biological and clinical information could transform the future of psychiatry Addresses fundamental questions and requirements for personalized psychiatry from a basic research and translational perspective This book offers a multidisciplinary look at the much-debated concept of “personalized medicine”. By combining a humanistic and a scientific approach, the book builds up a multidimensional way to understand the limits and potentialities of a personalized approach in medicine and healthcare. The book reflects on personalized medicine and complex diseases, the relationship between personalized medicine and the new bio-technologies, personalized medicine and personalized nutrition, and on some ethical, political, economic, and social implications of personalized medicine. This volume is of interest to researchers from several disciplines including philosophy, bio-medicine, and the social sciences. Chapter 16, “The Impact of Fantasy” is available open access under a Creative Commons Attribution 4.0 International License via link.springer.com. Cystic Fibrosis - Heterogeneity and Personalized Treatment provides the latest research and clinical evidence for clinicians, scientists and researchers involved in the care of patients with cystic fibrosis (CF). This book outlines the burden of the CF microbiome, utilisation of CF registries to impact future care, the sequelae of hepatobiliary complication, the use of upcoming technologies to provide patient-centred care, and provides an overview of cystic fibrosis transmembrane regulator (CFTR) modulators. Looking after patients with CF is highly rewarding, allowing those of us to combine our dedication and problem-solving skills to create a personalized approach. This book is invaluable for those involved in the care of CF patients. This book presents state of the art knowledge on severe asthma with the aim of providing readers with a clear understanding of, first, the heterogeneity of the condition and of patients’ symptom profiles and responses to therapy and, second, the future implications of this heterogeneity for individualized patient care. After an opening section that offers an overview of severe asthma, including its clinical significance, the pathogenesis, available diagnostic approaches, and treatment options are described in detail. The sections on diagnosis and treatment cover the role of biomarkers, the use of radiologic diagnostic modalities, and both pharmacologic and non-pharmacologic therapies, including emerging options that will address hitherto unmet needs of patients. The outcomes of cutting-edge preclinical and clinical research are carefully documented and numerous useful tips provided on patient management. The inclusion of many informative schematic figures will assist readers in grasping the contents easily. The book will be of high value for medical students, researchers, general physicians, specialists, and paramedical staff. Improved understanding of the cellular and molecular makeup of tumors in the last 30 years has unraveled a previously unexpected level of heterogeneity among tumor cells as well as within the tumor microenvironment. The concept of tumor heterogeneity underlines the realization that different tumors can display significant differences in their genomic content as well as in their overall behavior. Our capacity to better understand the heterogeneous make up of tumors has very important consequences on our ability to design efficient therapeutic strategies to improve patient survival. This book highlights several aspects of tumor heterogeneity in the context of metastatic development and summarize some of the challenges posed by heterogeneity for tumor diagnostics and therapeutic management of tumors. Individuals respond to pharmaceutical treatments differently due to the heterogeneity of patient populations. This heterogeneity can make it difficult to determine how efficacious or burdensome a treatment is for an individual patient. Personalized medicine involves using patient characteristics, therapeutics, or diagnostic testing to understand how individual patients respond to a given treatment. Personalized medicine increases the health impact of existing treatments by improving the matching process between patients and treatments and by improving a patient's understanding of the risk of serious side effects. In this paper, I compare the health impact of new treatment innovations with the potential health impact of personalized medicine. I find that the impact of personalized medicine depends on the number of treatments, the correlation between treatment effects, and the amount of noise in a patient's individual treatment effect signal. For multiple sclerosis treatments, I find that personalized medicine has the potential to increase the health impact of existing treatments by roughly 50 percent by informing patients of their individual treatment effect and risk of serious side effects. Personalized and precision medicine (PPM)—the targeting of therapies according to an individual’s genetic, environmental, or lifestyle characteristics—is becoming an increasingly important approach in health care treatment and prevention. The advancement of PPM is a challenge in traditional clinical, reimbursement, and regulatory landscapes because it is costly to develop and introduces a wide range of scientific, clinical, ethical, and socioeconomic issues. PPM raises a multitude of economic issues, including how information on accurate diagnosis and treatment success will be disseminated and who will bear the cost; changes to physician training to incorporate genetics, probability and statistics, and economic considerations; questions about whether the benefits of PPM will be confined to developed countries or will diffuse to emerging economies with less developed health care systems; the effects of patient heterogeneity on cost-effectiveness analysis; and opportunities for PPM’s growth beyond treatment of acute illness, such as prevention and reversal of chronic conditions. This volume explores the intersection of the scientific, clinical, and economic factors affecting the development of PPM, including its effects on the drug pipeline, on reimbursement of PPM diagnostics and treatments, and on funding of the requisite underlying research; and it examines recent empirical applications of PPM. This open access volume will introduce recent discoveries in cancer metabolism since the publication of the first edition in 2018, providing readers with an up-to-date understanding of developments in the field. Genetic alterations in cancer, in addition to being the fundamental drivers of tumorigenesis, can give rise to a variety of metabolic adaptations that allow cancer cells to survive and proliferate in diverse tumor microenvironments. This metabolic flexibility is different from normal cellular metabolic processes and leads to heterogeneity in cancer metabolism within the same cancer type or even within the same tumor. In this book, the authors delve into the complexity and diversity of cancer metabolism and highlight how understanding the heterogeneity of cancer metabolism is fundamental to the development of effective metabolism-based therapeutic strategies for cancer treatment. Deciphering how cancer cells utilize various nutrient resources will enable clinicians and researchers to pair specific chemotherapeutic agents with patients who are most likely to respond with positive outcomes, allowing for more cost-effective and personalized cancer treatment. This book has four major parts. Part one will cover the basic metabolism of cancer cells, followed by a discussion of the heterogeneity of cancer metabolism in part two. Part three addresses the relationship between cancer cells and cancer-associated fibroblasts, and the new part four will explore the metabolic interplay between cancer and other diseases. This new section makes the book unique from other texts currently available on the market. The second edition will be useful for cancer metabolism researchers, cancer biologists, epidemiologists, physicians, health care professionals in related disciplines, policymakers, marketing and economic strategists, among others. It may also be used in courses such as intro to cancer metabolism, cancer biology, and related biochemistry courses for undergraduate and graduate students. SPECTRUMS OF AMYOTROPHIC LATERAL SCLEROSIS Discover state-of-the-art research findings on ALS from leading authors and editors in the field In Spectrums of Amyotrophic Lateral Sclerosis: Heterogeneity, Pathogenesis & Therapeutic Directions, distinguished researchers and editors Dr. Christopher A. Shaw and Jessica R. Morrice deliver a practical and powerful perspective on Amyotrophic Lateral Sclerosis (ALS) as a heterogeneous spectrum of disorders. This increasingly accepted point-of-view allows researchers and medical professionals to develop better targeted interventions and more precise therapies. In the book, readers will find chapters on a wide variety of critical issues facing ALS researchers and healthcare practitioners treating ALS sufferers, including animal models of ALS, neuronal support cells known to have a pivotal role in ALS, and current challenges in ALS clinical trials, among others. The authors describe pathologic features common to all cases of ALS and why animal models, though crucial, should be interpreted with caution. Finally, multiple genetic and environmental etiologies of the disease are discussed. Readers will also benefit from the inclusion of: A thorough introduction to ALS as a spectrum disease and the implications for models, therapeutic development and clinical trial design Explorations of the genetic basis of ALS, prospective sALS etiologies, and the involvement of microbiome in ALS Discussions of ALS-PDC and environmental risk factors, protein aggregation in ALS, defects in RNA metabolism in ALS, and the non-cell autonomous nature of ALS and the involvement of glial cells Examinations of animal models of ALS and perspectives on previously failed ALS therapeutics and current therapeutic strategies Perfect for clinical neurologists, healthcare providers and caretakers, clinicians, and researchers studying motor neuron disease, Spectrums of Amyotrophic Lateral Sclerosis: Heterogeneity, Pathogenesis & Therapeutic Directions is also an indispensable resource for the neurodegenerative research community, neurology residents, and graduate-level neuroscience students. This book provides a clear and thorough

introduction to meta-analysis, the process of synthesizing data from a series of separate studies. Meta-analysis has become a critically important tool in fields as diverse as medicine, pharmacology, epidemiology, education, psychology, business, and ecology. Introduction to Meta-Analysis: Outlines the role of meta-analysis in the research process Shows how to compute effects sizes and treatment effects Explains the fixed-effect and random-effects models for synthesizing data Demonstrates how to assess and interpret variation in effect size across studies Clarifies concepts using text and figures, followed by formulas and examples Explains how to avoid common mistakes in meta-analysis Discusses controversies in meta-analysis Features a web site with additional material and exercises A superb combination of lucid prose and informative graphics, written by four of the world's leading experts on all aspects of meta-analysis. Borenstein, Hedges, Higgins, and Rothstein provide a refreshing departure from cookbook approaches with their clear explanations of the what and why of meta-analysis. The book is ideal as a course textbook or for self-study. My students, who used pre-publication versions of some of the chapters, raved about the clarity of the explanations and examples. David Rindskopf, Distinguished Professor of Educational Psychology, City University of New York, Graduate School and University Center, & Editor of the Journal of Educational and Behavioral Statistics. The approach taken by Introduction to Meta-analysis is intended to be primarily conceptual, and it is amazingly successful at achieving that goal. The reader can comfortably skip the formulas and still understand their application and underlying motivation. For the more statistically sophisticated reader, the relevant formulas and worked examples provide a superb practical guide to performing a meta-analysis. The book provides an eclectic mix of examples from education, social science, biomedical studies, and even ecology. For anyone considering leading a course in meta-analysis, or pursuing self-directed study, Introduction to Meta-analysis would be a clear first choice. Jesse A. Berlin, ScD Introduction to Meta-Analysis is an excellent resource for novices and experts alike. The book provides a clear and comprehensive presentation of all basic and most advanced approaches to meta-analysis. This book will be referenced for decades. Michael A. McDaniel, Professor of Human Resources and Organizational Behavior, Virginia Commonwealth University This volume comprehensively reviews oncology in the precision medicine era of personalized care, latest developments in the field, and indications and clinical trials for the treatment of cancer with targeted therapies, immunotherapy, and epigenetic modulators. It thoroughly addresses concerns of various types of cancers including cancers of the head and neck, lung, colon, esophagus, bladder, pancreas, and breast; melanoma; multiple myeloma; hepatocellular carcinoma; renal cell carcinoma; and sarcomas. It is organized and written in a format that is easy to follow for both clinicians and non-clinical scientists interested in personalized medicine. Chapters cover the identification of the clinical problem and summary of recent findings, tumor biology and heterogeneity, genomics, examples of simple and complex cases, biological pathways, future clinical trials, and financial considerations. Oncology in the Precision Medicine Era: Value-Based Medicine will serve as a useful resource for medical oncologists and healthcare providers tailoring medicine to the needs of the individual patient, from prevention and diagnosis to treatment and follow up. To determine if BRAF V600E is conserved during melanoma disease progression and the effect of heterogeneity on patient outcomes, clinical data was collected from 17 patients with cobas molecularly determined BRAF status. HRM analysis followed by Sanger sequencing was performed on tumor-rich regions micro-dissected from all available matched FFPE tissue samples from each patient to elucidate spatial and temporal differences in BRAF status. Notably, 4/7 patients (57%) were found to be misdiagnosed by the cobas test. Intra- and inter-tumor heterogeneity with respect to BRAF V600E was revealed in 6/13 patients (46%). Three patients had discordant results between primary and metastatic tumors, suggesting that BRAF is not necessary to initiate metastasis. In this cohort, patients harboring heterogeneous melanoma were found to have an increased likelihood of progressing or recurring during a given time period (HR 4.74, 95% CI 0.410-54.745, p = 0.1953) and were 3.566 times more likely to experience a new metastasis (95% CI 0.741-17.162, p = 0.0951) than patients with non-heterogeneous BRAF V600E melanoma. Our findings suggest a complex picture of melanoma pathogenesis whereby tumors are comprised of at least two distinct types of malignant clones that differ in BRAF mutation status and the presence of both negatively influences patient outcomes. Further investigation of melanoma heterogeneity is crucial to facilitate personalized treatment strategies for this aggressive malignancy. Genetic alterations in cancer, in addition to being the fundamental drivers of tumorigenesis, can give rise to a variety of metabolic adaptations that allow cancer cells to survive and proliferate in diverse tumor microenvironments. This metabolic flexibility is different from normal cellular metabolic processes and leads to heterogeneity in cancer metabolism within the same cancer type or even within the same tumor. In this book, we delve into the complexity and diversity of cancer metabolism, and highlight how understanding the heterogeneity of cancer metabolism is fundamental to the development of effective metabolism-based therapeutic strategies. Deciphering how cancer cells utilize various nutrient resources will enable clinicians and researchers to pair specific chemotherapeutic agents with patients who are most likely to respond with positive outcomes, allowing for more cost-effective and personalized cancer therapeutic strategies. The Year Book of Pathology and Laboratory Medicine brings you abstracts of the articles that reported the year's breakthrough developments in pathology and laboratory medicine, carefully selected from more than 300 journals worldwide. Expert commentaries evaluate the clinical importance of each article and discuss its application to your practice. There's no faster or easier way to stay informed! Chapters in this annual cover the most current information on all aspects of pathology and laboratory medicine including: molecular diagnostics, dermatopathology, anatomic pathology techniques, outcomes analysis, cytopathology, clinical immunology, clinical microbiology, neuropathology and hematology. Genetic diversity in solid tumors have critical consequences for tailoring personalized patient care. Treatments using chemo and/or radiation therapy has rendered the "one size fits all" model ineffective. Recent large-scale sequencing studies in cancers have shown that the overall mutational landscapes and tumor microenvironments can be distinct. These same studies have not largely focused on intra-tumoral heterogeneity. This expansive heterogeneity poses a major obstacle towards the personalization of treatment. Central to our approach in studying heterogeneity is the use of patient-derived xenograft (PDX). Our models,described herein, are poised to predict response to drug and radiation treatments in both individual and groups of patients with particular genetic constitutions. Our approach also combined mathematical and experimental models to study intratumoral diversity and evolution. We show that tumors genetic compositions can drift and under some circumstances, like the application of a selective pressure, can dramatically shift. Thus, the sampling of a tumor for genomic analyses in a fixed time and space offers only a geographically and temporally restricted view of its genetic composition. Our study on clonal evolution in cancers with BRAF mutations elucidates some of these principals. Namely,those that govern evolutionary dynamics of tumor subclones that we predict can confer resistance to our treatments. We describe our results on the subclonal architecture of non-small cell lung cancer (NSCLC) tumors containing cells with variants of the BRAF gene. We show that these distinct classes of tumor architecture have significant implications for targeted and genotoxic therapies. In an effort to expand our explanatory models beyond the genome, we show that distinct differentiation/epigenetic states within individual tumors contribute to substantial phenotypic variability. We use small cell lung cancer (SCLC), a tumor of neuroectodermal origin or the "primitive" epithelium, as our model. SCLC is an aggressive lung malignancy that often has initial dramatic responses to therapies but and almost invariably resists and rebounds after first-line treatments. Our approach involved the use of large transcriptomic datasets to identify new taxonomies regulating SCLC phenotypes which marked both tumoral and intratumoral heterogeneity. Taken together, these studies begin to elucidate the inter-tumor and intra-tumoral landscape of some cancers and the impact of this heterogeneity on therapeutic resistance in cancer. This User's Guide is a resource for investigators and stakeholders who develop and review observational comparative effectiveness research protocols. It explains how to (1) identify key considerations and best practices for research design; (2) build a protocol based on these standards and best practices; and (3) judge the adequacy and completeness of a protocol. Eleven chapters cover all aspects of research design, including: developing study objectives, defining and refining study questions, addressing the heterogeneity of treatment effect, characterizing exposure, selecting a comparator, defining and measuring outcomes, and identifying optimal data sources. Checklists of guidance and key considerations for protocols are provided at the end of each chapter. The User's Guide was created by researchers affiliated with AHRQ's Effective Health Care Program, particularly those who participated in AHRQ's DEcIDE (Developing Evidence to Inform Decisions About Effectiveness) program. Chapters were subject to multiple internal and external independent reviews. More more information, please consult the Agency website: www.effectivehealthcare.ahrq.gov) This important text/reference presents a comprehensive review of techniques for taxonomy matching, discussing matching algorithms, analyzing matching systems, and comparing matching evaluation approaches. Different methods are investigated in accordance with the criteria of the Ontology Alignment Evaluation Initiative (OAEI). The text also highlights promising developments and innovative guidelines, to further motivate researchers and practitioners in the field. Topics and features: discusses the fundamentals and the latest developments in taxonomy matching, including the related fields of ontology matching and schema matching; reviews next-generation matching strategies, matching algorithms, matching systems, and OAEI campaigns, as well as alternative evaluations; examines how the latest techniques make use of different sources of background knowledge to enable precise matching between repositories; describes the theoretical background, state-of-the-art research, and practical real-world applications; covers the fields of dynamic taxonomies, personalized directories, catalog segmentation, and recommender systems. This stimulating book is an essential reference for practitioners engaged in data science and business intelligence, and for researchers specializing in taxonomy matching and semantic similarity assessment. The work is also suitable as a supplementary text for advanced undergraduate and postgraduate courses on information and metadata management. This issue of PET Clinics focuses on PET-Based Molecular Imaging in Evolving Personalized Management Design, and is edited by Drs. Abass Alavi and Sandip Basu. Articles will include: PET-Based Personalized Medicine: An Unavoidable Path for the Foreseeable Future; Personalized Management Approaches in Lymphoma: Help from PET; PET-CT in Head-Neck Malignancies: the Implications for Personalized Clinical Practice; PET Imaging of Skeletal Metastases and its Role in Personalising Further Management; PET-Based Molecular Imaging in Designing a Personalized Management Model in Neuroendocrine Tumors; Personalized Clinical Decision Making in GI Malignancies: Where Can PET Help?; PET in Breast Carcinoma: Can it Aid in Developing a Personalized Treatment Design; PET and Thyroid Cancer: Can it Help in Evolving a Personalized Treatment Design?; PET Imaging Towards Individualized Management of Urological and Gynaecological Malignancies; The Possible Role of PET Imaging towards Individualized Management of Bone and Soft Tissue Malignancies; PET-Based Personalized Management of Inflammatory Disorders; PET-Based Radiation Oncology; PET-Based Interventional Radiology; The Current and Evolving Role of PET in Personalized Management of Lung Carcinoma, and more! This book provides a comprehensive overview of the current limitations and unmet needs in Hepatocellular Carcinoma (HCC) diagnosis, treatment, and prevention. It also provides newly emerging concepts, approaches, and technologies to address challenges. Topics covered include changing landscape of HCC etiologies in association with health disparities, framework of clinical management algorithm, new and experimental modalities of HCC diagnosis and prognostication, multidisciplinary treatment options including rapidly evolving molecular targeted therapies and immune therapies, multi-omics molecular characterization, and clinically relevant experimental models. The book is intended to assist collaboration between the diverse disciplines and facilitate forward and reverse translation between basic and clinical research by providing a comprehensive overview of relevant areas, covering epidemiological trend and population-level patient management strategies, new diagnostic and prognostic tools, recent advances in the standard care and novel therapeutic approaches, and new concepts in pathogenesis and experimental approaches and tools, by experts and opinion leaders in

their respective fields. By thoroughly and concisely covering whole aspects of HCC care, Hepatocellular Carcinoma serves as a valuable reference for multidisciplinary readers, and promotes the development of personalized precision care strategies that lead to substantial improvement of disease burden and patient prognosis in HCC. This book is a comprehensive guide to the techniques, clinical applications, and benefits of the different forms of liquid biopsy employed in patients with a variety of tumor types, including lung, breast and colorectal cancer. Offering detailed explanations, it discusses the how changes in tumors can be tracked using these cutting-edge technologies, which enable the detection and analysis of diverse circulating biomarkers: tumor cells, tumor DNA, tumor RNA (free or in exosomes), and fluid biomarkers identifiable by means of targeted proteomics. The use of such advanced technologies is enabling us to tackle questions and problems in a way that was not possible just a few years ago. We now have at our disposal an effective means of overcoming the problem of intratumor heterogeneity, which has limited the value of conventional biopsy approaches. As a consequence, oncology practice is about to change radically, toward truly personalized precision medicine. This book provides both clinicians and researchers with a thorough and up-to-date overview of progress in the field. Personalized pricing has become a reality through digitization. We examine firms' incentives to adopt one of the three pricing schemes: uniform, personalized, or group pricing in a Hotelling duopoly model. There are two types of consumer groups that are heterogeneous in their mismatch costs. We show that both firms employ personalized pricing in equilibrium regardless of the heterogeneity of consumer groups. If the consumer groups' heterogeneity is significant, the profits are higher when both firms use personalized pricing than when they employ uniform pricing; otherwise, the latter profits are higher than the former. Profits are highest when firms employ group pricing among the three cases. The ranking of consumer welfare among the three cases is opposite to that of profits. Genome heterogeneity-based personalized prevention Precision medicine holds great promise for the treatment of cancer and represents a unique opportunity for accelerated development and application of novel and repurposed therapeutic approaches. Current studies and clinical trials demonstrate the benefits of genomic profiling for patients whose cancer is driven by specific, targetable alterations. However, precision oncologists continue to be challenged by the widespread heterogeneity of cancer genomes and drug responses in designing personalized treatments. Chapters provide a comprehensive overview of the computational approaches, methods, and tools that enable precision oncology, as well as related biological concepts. Covered topics include genome sequencing, the architecture of a precision oncology workflow, and introduces cutting-edge research topics in the field of precision oncology. This book is intended for computational biologists, bioinformaticians, biostatisticians and computational pathologists working in precision oncology and related fields, including cancer genomics, systems biology, and immuno-oncology. Tumor heterogeneity refers to the existence of clonal subpopulations of cells within and between neoplastic lesions and is an important driver of tumor progression, resistance to therapy, and relapse. Precision medicine offers one strategy of combating tumor heterogeneity by using genetic information about these subpopulations to inform personalized therapy. Despite notable successes, the degree of heterogeneity in tumors is often too great for this "drug cocktail" approach to be effective, and patients frequently develop refractory or relapsed disease. Here we present an alternative approach to precision medicine, arguing that tumor heterogeneity can best be addressed by either (1) avoiding its emergence with early cancer detection or (2) combating it with equally heterogeneous therapies that leverage the naturally diverse repertoire of the adaptive immune system. To this end, we describe four technologies that address key limitations in the fields of early cancer detection and cancer immunotherapy. Beginning with early cancer detection, we first address the problem of biomarker scarcity by engineering an intravascular system of magnetic enrichment capable of collecting circulating cancer biomarkers from the entire blood volume. We continue by asking how we can overcome low signal-to-noise ratios in cancer liquid biopsies, and we present a method of enriching rare mutant alleles in cell-free DNA to enable more sensitive mutation detection. Acknowledging that there are inherent limitations to early detection using endogenous biomarkers, we also present an engineered immune cell sensor for ultrasensitive tumor detection in living subjects. Finally, we consider how we can leverage the body's natural immune diversity to theoretically cover all neoplastic clonal subpopulations. Using chimeric antigen receptor T-cell therapy and epitope spreading as an example, we present a method of delivering ectopic surface antigens to malignant cells to generate a universal approach to adoptive cell therapy in solid tumors. The approaches detailed in this thesis provide a conceptual framework for how to strategically approach translational cancer research and can inform continued efforts towards reducing the global burden of cancer. The burgeoning adoption of modern technologies provides a great opportunity for gathering multiple modalities of comprehensive personalized data on individuals. The thesis aims to address statistical challenges in analyzing these data, including patient-specific biomarkers, digital phenotypes and clinical data available from the electronic health records (EHRs) linked with other data sources to achieve precision medicine. The first part of the thesis introduces a dimension reduction method of microbiome data to facilitate subsequent analysis such as regression and clustering. We adopt the proposed zero-inflated Poisson factor analysis (ZIPFA) model on the Oral Infections, Glucose Intolerance and Insulin Resistance Study (ORIGINS) and provide valuable insights into the relation between subgingival microbiome and periodontal disease. The second part focuses on modeling the intensive longitudinal digital phenotypes collected by mobile devices. We develop a method based on a generalized state-space model to estimate the latent process of patient's health status. Cancer is a heterogeneous disease, which is reflected both on the cellular and the population level. Advances in detection, diagnosis, and treatment of malignancies have increased survival time of cancer patients; yet, the heterogeneity observed within and between tumors complicates accurate prognostication and interferes with efficacy of treatment. Heterogeneity is a global concept, mirrored for instance by the fact that the two vastly distinct cancer types discussed in this thesis - glioblastoma and colorectal cancer - are each characterized by high levels of tumor heterogeneity. Tumors have been recognized as ‘abnormal organs’ because transformed cells within one tumor exist in distinct states and intricately crosstalk with non-transformed cells in the tumor microenvironment. The term intra-tumor heterogeneity conceptualizes this notion. Inter-tumor heterogeneity refers to the fact that no tumor is like any other, which is illustrated most obviously by the comparison of tumors arising in different organs. The cells targeted for transformation, the transformation-initiating event, the environmental composition, and many more factors differ between neoplasms arising for instance in the brain (glioblastomas) and in the colon. Moreover, these parameters can also differ between tumors arising in the same organ, leading to the formation of distinct subtypes within a given type of cancer. Drivers of intra- and inter-tumor heterogeneity are the main focus of this thesis. Even though tumor heterogeneity presents a major challenge for the clinical management of individual patients, its presence allows the design of tailored therapeutic approaches and therefore exploring tumor heterogeneity holds promise for the design of personalized treatment strategies. This book is a quick reference guide to the new, more personalized approaches to the management of skin disorders that have emerged as a result of progress in our understanding of the genetic background and pathophysiology of skin diseases and the diversity of mechanisms underlying their clinical heterogeneity. A wide range of personalized and targeted therapies are described, including those for different skin cancers, chronic inflammatory skin diseases, and autoimmune diseases. In addition, readers will find that the book documents how research results in personalized medicine can be effectively transferred to dermatological practice and looks forward to future treatments that might be developed on the basis of recent research findings. The authors are all recognized experts in the field, and the text is presented in a reader-friendly format and well illustrated. Prostate cancer (CaP) is the most commonly diagnosed malignancy in men in the Western world. In North America, more than 275000 men are diagnosed annually whereby approximately 1 in 6 men will be diagnosed with CaP in their lifetime, and 1 in 34 men will die from castrate-resistant metastatic disease. Unfortunately, current clinical prognostic factors explain only a proportion of the observed variation in clinical outcome from patient to patient. Furthermore, over-treatment of indolent and low-risk cancers leads to inappropriate morbidity following radiotherapy or surgery. As such, better predictors of individualized prognosis and treatment response are urgently needed to triage patients to customized and intensified CaP treatment. Recent developments in next-generation sequencing have made it possible to identify prognostic and predictive signatures based on genomic profiles. Herein, we review the recent genetic data pertaining to prostate cancer carcinogenesis, progression, castrate-resistance and metastases. We discuss the genetic basis of CaP progression from localized to systemic disease (e.g. point mutations, copy number alterations and structural variants) and important considerations for CaP biology including intra- and inter-prostatic heterogeneity, multifocality and multiclonality, TMPRSS2–ERG and other ETS-family gene fusions and the role of the tumor microenvironment (e.g. hypoxia and the contribution of caner-associated stroma). Finally, we focus on the use of genomic markers as prognostic factors for local failure and for systemic disease, as novel risk stratification tools, in triaging patients to existing treatment options and, ultimately, the potential of genomics for the identification of molecular targets for CaP therapy. We conclude by summarizing selected outstanding questions in CaP biology that can be addressed effectively through international cooperation between genome sequencing projects such as The Cancer Genome Atlas (TCGA) and the International Cancer Genome Consortium (ICGC). Progress and Challenges in Precision Medicine presents an insightful overview to the myriad factors of personalized and precision medicine. The availability of the human genome, large amounts of data on individual genetic variations, environmental interactions, influence of lifestyle, and cutting-edge tools and technologies for big-data analysis have led to the age of personalized and precision medicine. Bringing together a global range of experts on precision medicine, this book collects previously scattered information into one concise volume which covers the most important developments so far in precision medicine and also suggests the most likely avenues for future development. The book includes clinical information, informatics, public policy implications, and information on case studies. It is a useful reference and background work for students, researchers, and clinicians working in the biomedical and medical fields, as well as policymakers in the health sciences. Provides an overview of the growing field of precision medicine Contains chapters from geographically diverse experts in their field Explores important aspects of precision medicine, including applications, ethics, and development This book contains a total of 21 chapters, each of which was written by experts in the corresponding field. The objective of this book is to provide a comprehensive and updated overview of cellular and molecular mechanisms underlying hypoxia's impacts on human health, as well as current advances and future directions in the detection, recognition, and management of hypoxia-related disorders. This collection of articles provides a clear update in the area of hypoxia research for biomedical researchers, medical students, nurse practitioners, and practicing clinicians in the fields of high altitude biology, cardiovascular biology and medicine, tumor oncology, obstetrics, pediatrics, and orthodontics and for others who may be interested in hypoxia. This book offers essential information on basic and translational research in gastric cancer, while also illustrating potential opportunities for its application in clinical practice. Gastric cancer is the fourth-most-common cancer globally and the second-leading cause of cancer deaths. It is known to be a heterogeneous disease with varied responses to “one-size-fits-all” treatments. Expanding our knowledge of cancer cell genetics may help us to explore more effective treatments in gastric cancer. The research on molecular mechanisms and its clinical applications, both presented here, will help readers gain an in-depth understanding of gastric cancer and its effective treatment. The book’s four sections cover personalized medicine, precise regional therapy, immunotherapy and nanomedicine in gastric cancer. Each part presents the state of art, recent advances and the authors’ experiences. Moreover, several interesting cases are described to demonstrate how gastric cancer patients benefit from translational research. This informative and attractively presented book on precision treatment in gastric cancer, including experimental findings and clinical treatment options, offers a valuable resource for oncologists and graduate students working in the field of gastric cancer. This book explains how analysis of the heterogeneity of chronic obstructive pulmonary disease (COPD) enhances understanding of the condition and leads to improved,

personalized treatment. State of the art knowledge is presented on a range of issues related to the heterogeneity of COPD, such as phenotypes (clinical, physiologic, radiologic, etc.), genotypes, and the tools to be used for dissecting heterogeneity (CT, MRI, biomarkers, etc.). Especially modern radiologic imaging holds promise in this context, and its role is described in detail with the aid of numerous illustrations. The implications of the heterogeneity for personalized treatment are clearly identified, with description of an appropriate tailored treatment strategy for each subgroup of patients. Information is provided on both current and emerging strategies, including bronchoscopic lung volume reduction and approaches to the management of pulmonary hypertension and comorbidities. This book will be a great asset in clinical practice and research for all who have an interest in COPD, a leading cause of morbidity and mortality worldwide. In this accessible collection, leading academic economists, psychologists and philosophers apply behavioural economic findings to practical policy concerns. Asthma is a chronic relapsing airways disease that represents a major public health problem worldwide. Intermittent exacerbations are provoked by airway mucosal exposure to pro-inflammatory stimuli, with RNA viral infections or inhaled allergens representing the two most common precipitants. In this setting, inducible signaling pathways the airway mucosa play a central role in the initiation of airway inflammation through production of antimicrobial peptides (defensins), cytokines, chemokines and arachidonic acid metabolites that coordinate the complex processes of vascular permeability, cellular recruitment, mucous hyper-secretion, bronchial constriction and tissue remodeling. These signals also are responsible for leukocytic infiltration into the submucosa, T helper-lymphocyte skewing, and allergic sensitization. Currently, it is well appreciated that asthma is a heterogeneous in terms of onset, exacerbants, severity, and treatment response. Current asthma classification methods are largely descriptive and focus on a single aspect or dimension of the disease. An active area of investigation on how to collect, use and visualize multidimensional profiling in asthma. This book will overview multidimensional profiling strategies and visualization approaches for phenotyping asthma. As an outcome, this work will facilitate the understanding of disease etiology, prognosis and/or therapeutic intervention. ? Personalized and precision medicine (PPM)—the targeting of therapies according to an individual's genetic, environmental, or lifestyle characteristics—is becoming an increasingly important approach in health care treatment and prevention. The advancement of PPM is a challenge in traditional clinical, reimbursement, and regulatory landscapes because it is costly to develop and introduces a wide range of scientific, clinical, ethical, and socioeconomic issues. PPM raises a multitude of economic issues, including how information on accurate diagnosis and treatment success will be disseminated and who will bear the cost; changes to physician training to incorporate genetics, probability and statistics, and economic considerations; questions about whether the benefits of PPM will be confined to developed countries or will diffuse to emerging economies with less developed health care systems; the effects of patient heterogeneity on cost-effectiveness analysis; and opportunities for PPM's growth beyond treatment of acute illness, such as prevention and reversal of chronic conditions. This volume explores the intersection of the scientific, clinical, and economic factors affecting the development of PPM, including its effects on the drug pipeline, on reimbursement of PPM diagnostics and treatments, and on funding of the requisite underlying research; and it examines recent empirical applications of PPM. A thorough and comprehensive guide to the theoretical, practical, and methodological approaches used in survey experiments across disciplines such as political science, health sciences, sociology, economics, psychology, and marketing This book explores and explains the broad range of experimental designs embedded in surveys that use both probability and non-probability samples. It approaches the usage of survey-based experiments with a Total Survey Error (TSE) perspective, which provides insight on the strengths and weaknesses of the techniques used. Experimental Methods in Survey Research: Techniques that Combine Random Sampling with Random Assignment addresses experiments on within-unit coverage, reducing nonresponse, question and questionnaire design, minimizing interview measurement bias, using adaptive design, trend data, vignettes, the analysis of data from survey experiments, and other topics, across social, behavioral, and marketing science domains. Each chapter begins with a description of the experimental method or application and its importance, followed by reference to relevant literature. At least one detailed original experimental case study then follows to illustrate the experimental method's deployment, implementation, and analysis from a TSE perspective. The chapters conclude with theoretical and practical implications on the usage of the experimental method addressed. In summary, this book: Fills a gap in the current literature by successfully combining the subjects of survey methodology and experimental methodology in an effort to maximize both internal validity and external validity Offers a wide range of types of experimentation in survey research with in-depth attention to their various methodologies and applications Is edited by internationally recognized experts in the field of survey research/methodology and in the usage of survey-based experimentation —featuring contributions from across a variety of disciplines in the social and behavioral sciences Presents advances in the field of survey experiments, as well as relevant references in each chapter for further study Includes more than 20 types of original experiments carried out within probability sample surveys Addresses myriad practical and operational aspects for designing, implementing, and analyzing survey-based experiments by using a Total Survey Error perspective to address the strengths and weaknesses of each experimental technique and method Experimental Methods in Survey Research: Techniques that Combine Random Sampling with Random Assignment is an ideal reference for survey researchers and practitioners in areas such political science, health sciences, sociology, economics, psychology, public policy, data collection, data science, and marketing. It is also a very useful textbook for graduate-level courses on survey experiments and survey methodology.