Contents

Preface Acknowledgments Contributors		v vii xiii
PA	rt I Background	
1	The Path to Oncology Drug Target Validation: An Industry Perspective Marta Cortés-Cros, Tobias Schmelzle, Volker M. Stucke, and Francesco Hofmann	3
PA	RT II DNA AS A TOOL TO MODULATE DRUG TARGETS	
2	Identification of Aptamers as Specific Binders and Modulators of Cell-Surface Receptor Activity	17
3	The Design and Structure–Functional Properties of DNA-Based Immunomodulatory Sequences	41
Pai	RT III RNA INTERFERENCE: FROM DESIGN TO DATA ANALYSIS	
4	siRNA Design Principles and Off-Target Effects	59
5	Western Blot Evaluation of siRNA Delivery by pH-Responsive Peptides Wanling Liang, A. James Mason, and Jenny K.W. Lam	73
6	High-Throughput RNAi Screening for the Identification of Novel Targets	89
7	Integration of RNAi and Small Molecule Screens to Identify Targets for Drug Development	97
8	CellProfiler and KNIME: Open Source Tools for High Content Screening	105
9	Holger Brandl, and Marc Bickle PARP Inhibition as a Prototype for Synthetic Lethal Screens	123

PART IV PROTEIN-FOCUSED TECHNOLOGIES

10	Structure-Based Target Druggability Assessment	141
11	Validating Pharmacological Disruption of Protein–Protein Interactions by Acceptor Photobleaching FRET Imaging Janos Roszik, Gábor Tóth, János Szöllősi, and György Vereb	165
12	Systematic Analysis of Complex Signal Transduction Pathways Using Protein Fragment Complementation Assays Thomas I. Koblizek, Ann Siehoff, and Anthony Pitt	179
13	Reverse Phase Protein Microarrays and Their Utility in Drug Development	187
Paf	AT V INNOVATIVE CELL CULTURE TECHNIQUES TO MIMIC TISSUE MICROENVIRONMENTS	
14	A Cell Culture System That Mimics Chronic Lymphocytic Leukemia Cells Microenvironment for Drug Screening and Characterization Alessandro Natoni, Michael O'Dwyer, and Corrado Santocanale	217
15	Two-Dimensional vs. Three-Dimensional In Vitro Tumor Migrationand Invasion AssaysMiriam Zimmermann, Carol Box, and Suzanne A. Eccles	227
16	Tumor Spheroid-Based Migration Assays for Evaluation of Therapeutic Agents	253
17	The Neurosphere Assay Applied to Neural Stem Cells and Cancer Stem Cells	267
Pai	RT VI GENETICALLY ENGINEERED ANIMAL MODELS TO STUDY GENE FUNCTIONS	
18	Genetically Engineered Animal Models for In Vivo Target Identification and Validation in Oncology Gemma Texidó	281
19	Target Validation in Mice by Constitutive and Conditional RNAi Aljoscha Kleinhammer, Wolfgang Wurst, and Ralf Kühn	307
20	In Vivo Target Validation by Inducible RNAi in Human Xenograft Mouse Models	325

PART VII TRANSLATIONAL METHODS TO VALIDATE BIOMARKERS

21	Bright-Field In Situ Hybridization Methods to Discover Gene Amplifications and Rearrangements in Clinical Samples	341
22	Combined MicroRNA In Situ Hybridization and Immunohistochemical Detection of Protein Markers Boye Schnack Nielsen and Kim Holmstrøm	353
Ind	lex	367