Study smart with Student Consult

THOMPSON & THOMPSON GENETICS EIGHTH EDITION IN MEDICINE















McInnes

Willard

ELSEVIER

Contents

CHAPTER 1

Introduction 1 The Birth and Development of Genetics and Genomics, 1 Genetics and Genomics in Medicine, 1 Omeard, 2

CHAPTER 2

Introduction to the Human Genome 3 The Human Genome and the Chromosomal Basis of Heredity, 3 Variation in the Human Genome, 11 Transmission of the Genome, 11 Human Gametogenesis and Fertilization, 18 Medical Relevance of Mitosis and Meiosis, 20

CHAPTER 3

The Human Genome:
Gene Structure and Function 21
Information Content of the Human Genome, 21
The Central Dogma: DNA → RNA → Protein, 22
Gene Organization and Structure, 24
Fundamentals of Gene Expression, 27
Gene Expression in Action, 29
Epigenetic and Epigenomic
Aspects of Gene Expression, 33
Gene Expression as the Integration
of Genomic and Epigenomic Signals, 35
Allelic Imbalance in Gene Expression, 36
Variation in Gene Expression
and Its Relevance to Medicine, 41

CHAPTER 4

Human Genetic Diversity:
Mutation and Polymorphism 43
The Nature of Genetic Variation, 43
inherited Variation and Polymorphism in DNA, 45
The Origin and Frequency
of Different Types of Mutations, 48
Types of Mutations and Their Consequences, 52
Variation in Individual Genomes, 54
Impact of Mutation and Polymorphism, 55

CHAPTER 5

Principles of Clinical Cytogenetics and Genome Analysis 57 Introduction to Cytogenetics and Genome Analysis, 57 Chromosome Abnormalities, 64 Chromosome and Genome Analysis in Cancer, 73

CHAPTER 6

The Chromosomal and Genomic Basis of Disease: Disorders of the Autosomes and Sex Chromosomes 75 Mechanisms of Abnormalities, 75 Aneuploidy, 75 Uniparental Discoury, 79 Genomic Disorders: Microdeletion and Duplication Syndromes, 80 Idiopathic Chromosome Abnormalities, 82 Segregation of Familial Abnormalities, 83 Disorders Associated with Genomic Imprinting, 85 The Sex Chromosomes and Their Abnormalities, 87 Disorders of Sex Development, 97 Neurodevelopmental Disorders and Intellectual Disability, 102

CHAPTER 7

Patterns of Single-Gene Inheritance 107 Overview and Concepts, 107 Pedigrees, 108 Mendelian Inheritance, 110 Autosomal Patterns of Mendelan Inbernance, 111 X-Linked Inheritance, 118 Pseudoantosomal Inheritance, 122 Mosaicism, 123 Parent-of-Origin Effects on Inheritance Patterns, 124 Dynamic Mutations: Unstable Repeat Expansions, 124 Maternal inheritance of Disorders Caused by Mutations in the Mitochondrial Genome, 128 Correlating Genotype and Phenotype, 130 Importance of the Family History in Medical Practice, 130

CHAPTER 8

Complex Inheritance of Common Multilactorial Disorders 133 Qualitative and Quantitative Traits, 133 Familial Aggregation and Correlation, 135 Determining the Relative Contributions of Genes and Environment to Complex Disease, 137 Examples of Common Multifactorial Diseases with a Genetic Contribution, 141 Examples of Multifactorial Traits for Which Specific Genetic and Environmental Factors are Known, 145 The Challenge of Multifactorial Disease with Complex Inheritance, 152

CHAPTER 9

х

Genetic Variation in Populations 155 Genotypes and Phenotypes in Populations, 155 Factors That Disturb Hardy-Weinberg Equilibrium, 158 Ethnic Differences in the Frequency of Various Genetic Diseases, 163 Genetics and Aucestry, 166

CHAPTER 10

Identifying the Geretic Basis for Human Disease 171 Genetic Basis for Linkage Analysis and Association, 171 Mapping Human Disease Genes, 178 From Gene Mapping to Gene Identification, 186 Finding Genes Responsible for Disease by Genome Sequencing, 189

CHAPTER 11

The Molecular Basis of Genetic Disease 195 The Effect of Mutation on Protein Function, 195 How Mutations Disrupt the Formation of Biologically Normal Proteins, 197 The Relationship Between Genotype and Phenotype in Genetic Disease, 197 The Hemoglobins, 198 The Hemoglobinopathies, 201

CHAPTER 12

The Molecular, Biachemical, and Celhilar Basis of Genetic Disease 215 Diseases Due to Mutations in Different Classes of Proteins, 215 Diseases Involving Enzymes, 216 Defects in Receptor Proteins, 226 Transport Defects, 230 Disorders of Structural Proteins, 233 Neurodegenerative Disorders, 242 Concluding Comments, 254

CHAPTER 13

The Treatment of Genetic Disease 257 The Current State of Treatment of Genetic Disease, 257 Special Considerations in Treating Genetic Disease, 259 Treatment by the Manipulation of Metabolism, 260 Treatment to Increase the Function of the Affected Gene or Protein, 263 Gene Therapy, 275 Precision Medicine: The Present and Future of the Treatment of Mendelian Disease, 289

CHAPTER 14

Developmental Genetics and Birth Defects 283 (With the assistance of Anthony Wynshaw-Boris, MD, PhD)

Developmental Biology in Medicine, 283 Introduction to Developmental Biology, 287 Genes and Environment in Development, 289 Easic Concepts of Developmental Biology, 290 Cellular and Molecular Mechanisms in Development, 300 Interaction of Developmental Mechanisms in Embryogenesis, 306 Concluding Comments, 307

CHAPTER 15

Cancer Genetics and Genomics 309 Neoplasia, 309 Genetic Basis of Cancer, 309 Cancer in Families, 314 Familial Occurrence of Cancer, 323 Sporadic Cancer, 323 Gytogenetic Changes in Cancer, 327 Applying Genomics to Individualize Cancer Therapy, 327 Cancer and the Environment, 330

CHAPTER 16

Risk Assessment and Genetic Counseling 333 Family History in Rish Assessment, 333 Genetic Counseling in Clinical Practice, 334 Determining Recurrence Risks, 336 Empirical Recurrence Risks, 342 Molecular and Genome Based Diagnostics, 344

CHAPTER 17

Prenaral Diagnosis and Screening 349 Methods of Prenatal Diagnosis, 350 Indications for Prenatal Diagnosis by Invasive Testing, 355 Prenatal Screening, 356 Laboratory Studies, 361 Genetic Counseling for Prenatal Diagnosis and Screening, 365

CHAPTER 18

Application of Genomics to
 Medicine and Personalized Health Care 369
 Genetic Screening in Populations, 369
 Pharmacogenomics, 372
 Pharmacogenomics as a Complex Trait, 375
 Screening for Genetic
 Susceptibility to Disease, 375
 Personalized Genomic Medicine, 380

CONTENTS xi

CHAPTER 19 Ethical and Social Issues in Genetics and Genomics 383 Principles of Biomedical Ethics, 383 Ethical Dilemmas Arising in Medical Genetics, 383 Privacy of Genetic Information, 386 Eugenic and Dysgenic Effects of Medical Genetics, 388 Genetics in Medicine, 390 CASES Clinical Case Studies Ellustrating Genetic Principles .397 Glossary 489

Sources and Acknowledgments 509

Answers to Problems 515

Index 533