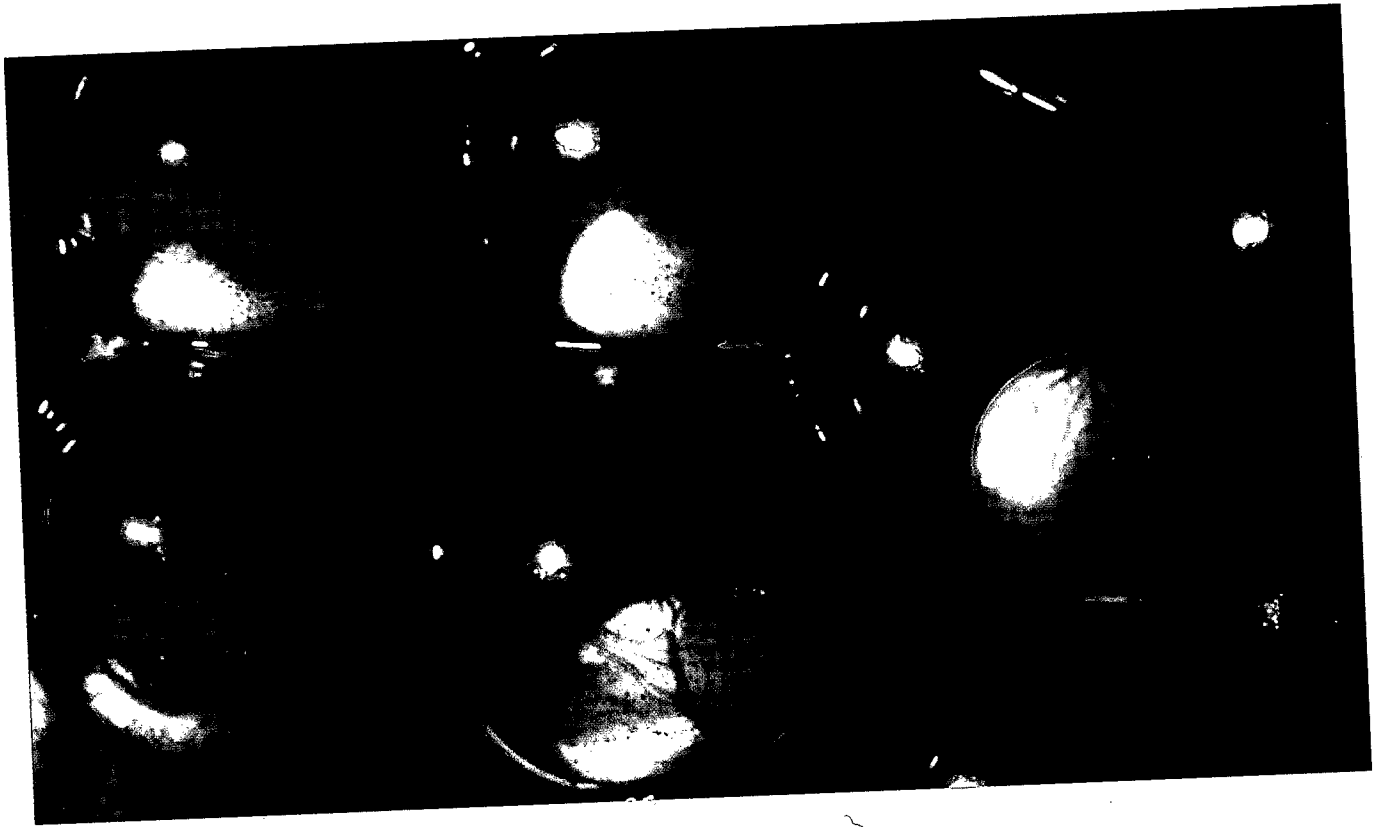


Developmental Biology

NINTH EDITION



SCOTT F. GILBERT

Swarthmore College and The University of Helsinki

Universitäts- und Landes-
bibliothek. Darmstadt
Bibliothek Biologie

Inv.-Nr. 16872
.....



Sinauer Associates, Inc. • Publishers • Sunderland, Massachusetts USA

Contents

PART I QUESTIONS Introducing Developmental Biology 1

CHAPTER 1

Developmental Anatomy 5

The Cycle of Life 6

A Frog's Life 6

Gametogenesis and fertilization 6

Cleavage and gastrulation 7

Organogenesis 10

Metamorphosis and gametogenesis 11

"How Are You?" 12

Comparative embryology 12

Epigenesis and preformation 12

Naming the parts: The primary germ layers and early organs 14

The four principles of Karl Ernst von Baer 16

Keeping Track of Moving Cells: Fate Maps and Cell Lineages 17

Fate maps 19

Direct observation of living embryos 19

Dye marking 19

Genetic labeling 20

Transgenic DNA chimeras 22

Evolutionary Embryology 23

Embryonic homologies 24

Medical Embryology and Teratology 27

Genetic malformations and syndromes 27

Disruptions and teratogens 28

CHAPTER 2

Developmental Genetics 31

Evidence for Genomic Equivalence 32

■ **SIDELIGHTS & SPECULATIONS** The Basic Tools of Developmental Genetics 32

Differential Gene Transcription 35

Anatomy of the gene: Active and repressed chromatin 36

Anatomy of the gene: Exons and introns 37

Anatomy of the gene: Promoters and enhancers 39

Transcription factor function 42

■ **SIDELIGHTS & SPECULATIONS** Reprogramming Cells: Changing Cell Differentiation through Embryonic Transcription Factors 45

DNA Methylation and the Control of Transcription 48

Mechanisms by which DNA methylation blocks transcription 49

Inheritance and stabilization of DNA methylation patterns 49

■ **SIDELIGHTS & SPECULATIONS** Consequences of DNA Methylation 50

Differential RNA Processing 53

Control of early development by nuclear RNA selection 53

Creating families of proteins through differential mRNA splicing 54

Splicing enhancers and recognition factors 56

Control of Gene Expression at the Level of Translation 58

Differential mRNA longevity 58

Selective inhibition of mRNA translation: Stored oocyte mRNAs 58

microRNAs: Specific regulators of mRNA translation and transcription 61

■ **SIDELIGHTS & SPECULATIONS** microRNAs in Transcriptional Gene Regulation 63

Control of RNA expression by cytoplasmic localization 64

Stored mRNAs in brain cells 65

Posttranslational regulation of gene expression 66

CHAPTER 3

Cell-Cell Communication in Development 69

Cell Adhesion 70

Differential cell affinity 70

The thermodynamic model of cell interactions 72

Cadherins and cell adhesion 73

■ **SIDELIGHTS & SPECULATIONS** Shape Change and Epithelial Morphogenesis: "The Force Is Strong in You" 76

Cell Migration 78

Cell Signaling 79

Induction and competence 79

Cascades of induction: Reciprocal and sequential inductive events 80

Instructive and permissive interactions 81

Epithelial-mesenchymal interactions 82

Paracrine Factors: The Inducer Molecules 84

Signal transduction cascades: The response to inducers 85

Fibroblast growth factors and the RTK pathway 85

The JAK-STAT pathway 88

The Hedgehog family 90

The Wnt family 92

The TGF- β superfamily 94

Other paracrine factors 95

■ **SIDELIGHTS & SPECULATIONS** Cell Death Pathways 96

Juxtacrine Signaling 98

The Notch pathway: Juxtaposed ligands and receptors 98

■ **SIDELIGHTS & SPECULATIONS** Juxtacrine Signaling and Cell Patterning 99

Maintaining the Differentiated State 101

The Extracellular Matrix as a Source of Developmental Signals 102

Integrins: Receptors for extracellular matrix molecules 102

Epithelial-Mesenchymal Transition 105

PART

SPECIFICATION Introducing Cell Commitment and Early Embryonic Development 109

Levels of Commitment 109

Autonomous Specification 110

Conditional Specification 112

Morphogen Gradients and Cell Specification 116

Syncytial Specification 117

Summary 119

CHAPTER 4

Fertilization: Beginning a New Organism 121

Structure of the Gametes 121

Sperm 121

The egg 125

Recognition of egg and sperm 127

External Fertilization in Sea Urchins 127

Sperm attraction: Action at a distance 128

The acrosome reaction 130

Recognition of the egg's extracellular coat 131

Fusion of the egg and sperm cell membranes 133

The fast block to polyspermy 135

The slow block to polyspermy 136

Calcium as the initiator of the cortical granule reaction 137

Activation of Egg Metabolism in Sea Urchins 139

Release of intracellular calcium ions 139

Effects of calcium 142

■ **SIDELIGHTS & SPECULATIONS** Rules of Evidence: "Find It, Lose It, Move It" 144

Fusion of genetic material 145

Internal Fertilization in Mammals 145

Getting the gametes into the oviduct: Translocation and capacitation 145

In the vicinity of the oocyte: Hyperactivation, thermotaxis, and chemotaxis 148

Recognition at the zona pellucida 149

Gamete fusion and the prevention of polyspermy 152

Fusion of genetic material 153

■ **SIDELIGHTS & SPECULATIONS** The Nonequivalence of Mammalian Pronuclei 154

Activation of the mammalian egg 155

Coda 155

CHAPTER 5**Early Development in Selected Invertebrates 159****EARLY DEVELOPMENTAL PROCESSES: AN OVERVIEW 159****Cleavage 159**

From fertilization to cleavage 160

The cytoskeletal mechanisms of mitosis 161

Patterns of embryonic cleavage 162

Gastrulation 162**Cell Specification and Axis Formation 164****EARLY DEVELOPMENT IN SEA URCHINS 165****Sea Urchin Cleavage 165**

Blastula formation 166

Fate maps and the determination of sea urchin blastomeres 166

Global regulatory networks and skeletogenic mesenchyme specification 167

Specification of the vegetal cells 171

Axis specification 172

Sea Urchin Gastrulation 172

Ingression of the skeletogenic mesenchyme 172

Invagination of the archenteron 176

EARLY DEVELOPMENT IN SNAILS 178**Cleavage in Snail Embryos 178**

The snail fate map 181

The polar lobe: Cell determination and axis formation 182

Gastrulation in Snails 185■ **SIDELIGHTS & SPECULATIONS** Adaptation by Modifying Embryonic Cleavage 186**EARLY DEVELOPMENT IN TUNICATES 187****Tunicate Cleavage 187**

The tunicate fate map 187

Autonomous and conditional specification of tunicate blastomeres 188

Specification of the embryonic axes 191

Gastrulation in Tunicates 191**THE NEMATODE *C. ELEGANS* 192****Cleavage and Axis Formation in *C. elegans* 193**Rotational cleavage of the *C. elegans* egg 193

Anterior-posterior axis formation 193

Formation of the dorsal-ventral and right-left axes 196

Control of blastomere identity 197

Gastrulation in *C. elegans* 199

Coda 200

CHAPTER 6**The Genetics of Axis Specification in *Drosophila* 203****EARLY DROSOPHILA DEVELOPMENT 204****Fertilization 204****Cleavage 204**

The mid-blastula transition 205

Gastrulation 206**GENES THAT PATTERN THE DROSOPHILA BODY PLAN 208****Primary Axis Formation during Oogenesis 209**

Anterior-posterior polarity in the oocyte 209

Dorsal-ventral patterning in the oocyte 211

Generating the Dorsal-Ventral Pattern in the Embryo 213

Dorsal, the ventral morphogen 213

Establishing a nuclear Dorsal gradient 214

Effects of the Dorsal protein gradient 214

■ **SIDELIGHTS & SPECULATIONS** The Left-Right Axis 217**Segmentation and the Anterior-Posterior Body Plan 218**

Maternal gradients: Polarity regulation by oocyte cytoplasm 219

The molecular model: Protein gradients in the early embryo 219

The anterior organizing center: The Bicoid and Hunchback gradients 223

The terminal gene group 225

Summarizing early anterior-posterior axis specification in *Drosophila* 226

Segmentation Genes 226

■ **SIDELIGHTS & SPECULATIONS** Segments and Parasegments 227

The gap genes 228

The pair-rule genes 229

The segment polarity genes 231

The Homeotic Selector Genes 234

Initiating and maintaining the patterns of homeotic gene expression 235

Realisator genes 236

Axes and Organ Primordia: The Cartesian Coordinate Model 236

Coda 237

CHAPTER 7

Amphibians and Fish: Early Development and Axis Formation 241

EARLY AMPHIBIAN DEVELOPMENT 242

Fertilization, Cortical Rotation, and Cleavage 242

Unequal radial holoblastic cleavage 243

The mid-blastula transition: Preparing for gastrulation 244

Amphibian Gastrulation 244

Vegetal rotation and the invagination of the bottle cells 245

■ **SIDELIGHTS & SPECULATIONS** Fibronectin and the Pathways for Mesodermal Migration 250

Epiboly of the prospective ectoderm 251

Progressive Determination of the Amphibian Axes 252

Hans Spemann: Inductive interactions in regulative development 253

Hans Spemann and Hilde Mangold: Primary embryonic induction 255

Molecular Mechanisms of Amphibian Axis Formation 256

How does the organizer form? 257

Functions of the organizer 262

Induction of neural ectoderm and dorsal mesoderm: BMP inhibitors 263

Epidermal inducers: The BMPs 265

■ **SIDELIGHTS & SPECULATIONS** BMP4 and Geoffroy's Lobster 267

The Regional Specificity of Neural Induction 267

The head inducer: Wnt inhibitors 268

Trunk patterning: Wnt signals and retinoic acid 270

Specifying the Left-Right Axis 272

EARLY ZEBRAFISH DEVELOPMENT 273

Cleavage 275

Gastrulation and Formation of the Germ Layers 277

Axis Formation in Zebrafish 278

Dorsal-ventral axis formation 278

The fish Nieuwkoop center 281

Anterior-posterior axis formation 282

Left-right axis formation 282

Coda 283

CHAPTER 8

Birds and Mammals: Early Development and Axis Formation 287

EARLY DEVELOPMENT IN BIRDS 287

Cleavage 287

Gastrulation of the Avian Embryo 288

The hypoblast 288

The primitive streak 288

Molecular mechanisms of migration through the primitive streak 292

Regression of the primitive streak and epiboly of the ectoderm 293

Axis Specification and the Avian "Organizer" 295

The role of gravity and the PMZ 295

The chick "organizer" 296

Anterior-posterior patterning 297

Left-right axis formation 298

EARLY MAMMALIAN DEVELOPMENT 300

Cleavage 300

The unique nature of mammalian cleavage 300

Compaction 301

■ **SIDELIGHTS & SPECULATIONS** Trophoblast or ICM? 302

Escape from the zona pellucida 304

Mammalian Gastrulation 304

Modifications for development inside another organism 305

Formation of the extraembryonic membranes 307

■ **SIDELIGHTS & SPECULATIONS** Twins and Chimeras 309

Mammalian Axis Formation 311

The anterior-posterior axis: Two signaling centers 311

Anterior-posterior patterning by FGF and retinoic acid gradients 312

Anterior-posterior patterning: The Hox code hypothesis 314

Experimental analysis of the Hox code 315

The Dorsal-Ventral and Left-Right Axes 316

The dorsal-ventral axis 316

The left-right axis 317

Coda 319

PART III THE STEM CELL CONCEPT Introducing Organogenesis 323

The Stem Cell Concept 323

Stem Cell Vocabulary 326

Adult Stem Cells 327

Adult Stem Cell Niches 328

Mesenchymal Stem Cells: Multipotent

Adult Stem Cells 330

A New Perspective on Organogenesis 331

CHAPTER 9

The Emergence of the Ectoderm: Central Nervous System and Epidermis 333

Establishing the Neural Cells 333

CONSTRUCTING THE CENTRAL NERVOUS SYSTEM 334

Formation of the Neural Tube 334

Primary neurulation 335

Secondary neurulation 340

BUILDING THE BRAIN 341

Differentiation of the Neural Tube 341

The anterior-posterior axis 341

The dorsal-ventral axis 343

Differentiation of Neurons in the Brain 345

Tissue Architecture of the Central Nervous System 348

Spinal cord and medulla organization 349

Cerebellar organization 350

Cerebral organization 351

■ **SIDELIGHTS & SPECULATIONS** Adult Neural Stem Cells 354

■ **SIDELIGHTS & SPECULATIONS** The Unique Development of the Human Brain 356

DEVELOPMENT OF THE VERTEBRATE EYE 359

The Dynamics of Optic Development 359

Formation of the Eye Field 359

Cell Differentiation in the Vertebrate Eye 362

Neural retina differentiation 362

Lens and cornea differentiation 364

THE EPIDERMIS AND ITS CUTANEOUS APPENDAGES 365

Origin of the Epidermis 365

The Cutaneous Appendages 366

■ **SIDELIGHTS & SPECULATIONS** EDAR Syndromes 369

CHAPTER 10

Neural Crest Cells and Axonal Specificity 373

THE NEURAL CREST 373

Specification of Neural Crest Cells 374

Regionalization of the Neural Crest 376

Trunk Neural Crest 377

Migration pathways of trunk neural crest cells 377

The mechanisms of trunk neural crest migration 378

The ventral pathway 379

The dorsolateral migration pathway 382

Cranial Neural Crest 383

Intramembranous ossification: Neural crest-derived head skeleton 385

Coordination of face and brain growth 387

Tooth formation 388

Cardiac Neural Crest 388

Cranial Placodes 389

- *SIDELIGHTS & SPECULATIONS* Cranial Neural Crest Cell Migration and Specification 391

NEURONAL SPECIFICATION AND AXONAL SPECIFICITY 392

The Generation of Neuronal Diversity 393

Pattern Generation in the Nervous System 394

- Cell adhesion and contact guidance by attraction and repulsion 396
- Guidance by diffusible molecules 398
- Target selection 399
- Forming the synapse: Activity-dependent development 402
- Differential survival after innervation: Neurotrophic factors 403

- *SIDELIGHTS & SPECULATIONS* The Brainbow 404

- Paths to glory: The travels of the retinal ganglion axons 404

The Development of Behaviors: Constancy and Plasticity 408

CHAPTER 11

Paraxial and Intermediate Mesoderm 413

PARAXIAL MESODERM: THE SOMITES AND THEIR DERIVATIVES 414

Formation of the Somites 415

- Periodicity of somite formation 417
- Where somites form: The Notch pathway 417

- *SIDELIGHTS & SPECULATIONS* Coordinating Waves and Clocks in Somite Formation 419

- Separation of somites from the unsegmented mesoderm 420
- Epithelialization of the somites 420
- Somite specification along the anterior-posterior axis 420
- Differentiation of the somites 421
- Determination of the sclerotome 424
- Determination of the central dermamyotome 425
- Determination of the myotome 425

Myogenesis: The Generation of Muscle 426

- Myogenic bHLH proteins 426
- Specification of muscle progenitor cells 426
- Myoblast fusion 427

Osteogenesis: The Development of Bones 428

- Endochondral ossification 428

- Vertebrae formation 431

Dorsal Aorta Formation 432

Tendon Formation: The Syndetome 432

INTERMEDIATE MESODERM: THE UROGENITAL SYSTEM 434

The Progression of Kidney Types 434

Specification of the Intermediate Mesoderm: Pax2/8 and Lim1 435

Reciprocal Interactions of Developing Kidney Tissues 436

- Mechanisms of reciprocal induction 437

Coda 442

CHAPTER 12

Lateral Plate Mesoderm and the Endoderm 445

LATERAL PLATE MESODERM 445

Heart Development 446

- Specification of heart tissue 446
- Migration of cardiac precursor cells 448
- Determination of anterior and posterior cardiac domains 450
- Heart cell differentiation 450
- Fusion of the heart rudiments and initial heartbeats 452
- Looping and formation of heart chambers 453

- *SIDELIGHTS & SPECULATIONS* Redirecting Blood Flow in the Newborn Mammal 455

Formation of Blood Vessels 456

- Constraints on the construction of blood vessels 456
- Vasculogenesis: The initial formation of blood vessels 458
- Angiogenesis: Sprouting of blood vessels and remodeling of vascular beds 461
- Arterial and venous differentiation 462
- Organ-specific capillary formation 463
- Anti-angiogenesis in normal and abnormal development 465
- The lymphatic vessels 465

Hematopoiesis: The Stem Cell Concept 466

- Sites of hematopoiesis 466
- Committed stem cells and their fates 468
- Hematopoietic inductive microenvironments 470
- Stem cell niche construction 470

ENDODERM 471**The Pharynx 471****The Digestive Tube and Its Derivatives 473**

Specification of the gut tissue 473

Liver, pancreas, and gallbladder 475

- **SIDELIGHTS & SPECULATIONS** Specification of Liver and Pancreas 476

The Respiratory Tube 478**The Extraembryonic Membranes 480**

The amnion and chorion 481

The allantois and yolk sac 482

CHAPTER 13**Development of the Tetrapod Limb 485****Formation of the Limb Bud 486**

Specification of the limb fields 486

Induction of the early limb bud: Wnt proteins and fibroblast growth factors 488

Specification of forelimb or hindlimb 488

Generating the Proximal-Distal Axis of the Limb 491

The apical ectodermal ridge 491

FGFs in the induction of the AER 492

Specifying the limb mesoderm: Determining the proximal-distal polarity of the limb 493

A reaction-diffusion model for limb specification 494

Specification of the Anterior-Posterior Axis 495

The zone of polarizing activity 495

- **SIDELIGHTS & SPECULATIONS** Hox Gene Changes during Limb Development 498

Specifying digit identity by Sonic hedgehog 500

Generation of the Dorsal-Ventral Axis 502**Coordinating the Three Axes 502****Cell Death and the Formation of Digits and Joints 504**

Sculpting the autopod 504

- **SIDELIGHTS & SPECULATIONS** Limb Development and Evolution 505

Forming the joints 507

Continued Limb Growth: Epiphyseal Plates 508

Fibroblast growth factor receptors: Dwarfism 508

Growth hormone and estrogen receptors 509

Parathyroid hormone-related peptide and Indian hedgehog 509

Coda 509**CHAPTER 14****Sex Determination 511****CHROMOSOMAL SEX DETERMINATION 512****The Mammalian Pattern: Primary and Secondary Sex Determination 512****Primary Sex Determination in Mammals 513**

The developing gonads 513

Mechanisms of mammalian primary sex determination: Making decisions 515

The ovary pathway: Wnt4 and R-spondin1 517

The testis pathway 518

The right time and the right place 521

- **SIDELIGHTS & SPECULATIONS** Mysteries of Gonad Differentiation 521

Secondary Sex Determination in Mammals: Hormonal Regulation of the Sexual Phenotype 523

The genetic analysis of secondary sex determination 523

Brain sex: Secondary sex determination through another pathway? 525

- **SIDELIGHTS & SPECULATIONS** Brain Sex: Sex Determinants and Behaviors in Mice and Rats 526

Chromosomal Sex Determination in *Drosophila* 529The *Sex-lethal* gene 529*Doublesex*: The switch gene for sex determination 532Brain sex in *Drosophila* 533**Dosage Compensation 534****ENVIRONMENTAL SEX DETERMINATION 534****Temperature-Dependent Sex Determination in Reptiles 534**

The aromatase hypothesis for environmental sex determination 535

Estrogens, aromatase, sex reversal, and conservation biology 535

Location-Dependent Sex Determination 536**Coda 538**

CHAPTER 15

**Postembryonic Development:
Metamorphosis, Regeneration,
and Aging 541****METAMORPHOSIS: THE HORMONAL
REACTIVATION OF DEVELOPMENT 541****Amphibian Metamorphosis 542**

Morphological changes associated with amphibian metamorphosis 542

Hormonal control of amphibian metamorphosis 545

Regionally specific developmental programs 547

- **SIDELIGHTS & SPECULATIONS** Variations on the Theme of Amphibian Metamorphosis 548

Metamorphosis in Insects 550

Imaginal discs 551

Determination of the wing imaginal discs 554

Hormonal control of insect metamorphosis 556

The molecular biology of 20-hydroxyecdysone activity 556

REGENERATION 560**Epimorphic Regeneration of Salamander
Limbs 561**

Formation of the apical ectodermal cap and regeneration blastema 561

Proliferation of the blastema cells: The requirement for nerves and the AEC 563

- **SIDELIGHTS & SPECULATIONS** How Do the Blastema Cells Know Their Proximal and Distal Levels? 564

Morphallactic Regeneration in *Hydra* 566

The head activation gradient 567

The head inhibition gradient 567

The hypostome as an "organizer" 568

The basal disc activation and inhibition gradients 569

**Compensatory Regeneration in the Mammalian
Liver 570****AGING: THE BIOLOGY OF SENESCENCE 571****Genes and Aging 571**

Genes encoding DNA repair proteins 571

Aging and the insulin signaling cascade 573

Integrating the conserved aging pathways 575

**Environmental and Epigenetic Causes
of Aging 575**

- **SIDELIGHTS & SPECULATIONS** Exceptions to the Aging Rule 579

Promoting longevity 579

CHAPTER 16

The Saga of the Germ Line 583**Germ Plasm and the Determination of the
Primordial Germ Cells 583**

Germ cell determination in nematodes 584

Germ cell determination in insects 585

Germ cell determination in frogs and fish 588

Germ cell determination in mammals 588

The inert genome hypothesis 589

- **SIDELIGHTS & SPECULATIONS** Pluripotency, Germ Cells, and Embryonic Stem Cells 590

Germ Cell Migration 592Germ cell migration in *Drosophila* 592

Germ cell migration in vertebrates 594

Meiosis 598

- **SIDELIGHTS & SPECULATIONS** Big Decisions: Mitosis or Meiosis? Sperm or Egg? 600

Gamete Maturation 602

Maturation of the oocytes in frogs 603

Gene transcription in amphibian oocytes 604

Meroistic oogenesis in insects 606

Gametogenesis in Mammals 607

Spermatogenesis 607

Oogenesis 610

Coda 613

PART IV SYSTEMS BIOLOGY Expanding Developmental Biology to Medicine, Ecology, and Evolution 617

Context-Dependent Properties 619
Emergence 619
Level-Specific Rules 620

Heterogeneous Causation 620
Integration 621
Modules and Robustness 622

CHAPTER 17

Medical Aspects of Developmental Biology 625

DISEASES OF DEVELOPMENT 626

Genetic Errors of Human Development 626
The Nature of Human Syndromes 627
Genetic Heterogeneity and Phenotypic Heterogeneity 628

Teratogenesis: Environmental Assaults on Human Development 628

■ **SIDELIGHTS & SPECULATIONS** Prenatal Diagnosis and Preimplantation Genetics 629

Alcohol as a teratogen 631
Retinoic acid as a teratogen 633
Endocrine disruptors 634
Other teratogenic agents 639

■ **SIDELIGHTS & SPECULATIONS** Testicular Dysgenesis Syndrome and the Transgenerational Effects of Endocrine Disruptors 640

Cancer as a Disease of Development 643

Context-dependent tumors 643
The cancer stem cell hypothesis: Cancer as a disease of stem cell regulation 644
Cancer as a return to embryonic invasiveness: Migration reactivated 645
Cancer and epigenetic gene regulation 645

■ **SIDELIGHTS & SPECULATIONS** The Embryonic Origins of Adult-Onset Illnesses 646

DEVELOPMENTAL THERAPIES 648

Anti-Angiogenesis 648

Stem Cells and Tissue Regeneration 649

Embryonic stem cells 649
Induced pluripotent stem cells 651

Adult stem cells and regeneration therapy 653
Direct transdifferentiation 655
Coda 655

CHAPTER 18

Developmental Plasticity and Symbiosis 659

The Environment as a Normal Agent in Producing Phenotypes 659

Diet-induced polyphenisms 661
Predator-induced polyphenisms 663
Temperature as an environmental agent 664

Environmental Induction of Behavioral Phenotypes 667

Adult anxiety and environmentally regulated DNA methylation 667

Learning: The Developmentally Plastic Nervous System 667

Experiential changes in mammalian visual pathways 668

Life Cycles and Polyphenisms 670

Diapause 670
Larval settlement 670
The spadefoot toad: A hard life 671

■ **SIDELIGHTS & SPECULATIONS** Life Cycle Choices: *Dictyostelium* 672

Developmental Symbioses 675

Mechanisms of developmental symbiosis: Getting the partners together 676
The *Euprymna-Vibrio* symbiosis 677
Obligate developmental mutualism 677
Symbiosis in the mammalian intestine 678

Coda 680

CHAPTER 19

Developmental Mechanisms of Evolutionary Change 683

**"Unity of Type" and "Conditions of Existence":
Charles Darwin's Synthesis** 683

**Preconditions for Evolution through
Developmental Change** 684

Modularity: Divergence through dissociation 684

Molecular parsimony: Gene duplication and
divergence 686

Deep Homology 688

Mechanisms of Evolutionary Change 689

Heterotopy 689

Heterochrony 691

Heterometry 692

Heterotypy 696

Developmental Constraints on Evolution 697

Physical constraints 697

Morphogenetic constraints: The reaction-diffusion
model 697

Phyletic constraints 700

Selectable Epigenetic Variation 702

Transgenerational inheritance of environmentally
induced traits 702

Genetic assimilation 705

■ **SIDELIGHTS & SPECULATIONS** Hsp90 and Genetic
Assimilation 706

Fixation of environmentally induced
phenotypes 708

A Developmental Account of Evolution 709

Glossary G-1

Chapter-Opening Credits C-1

Author Index A-1

Subject Index S-1