

# Contents

<b>Introduction.</b> LUTZ NOVER and LAWRENCE HIGHTOWER .....	1
--	---

## Part I Heat Shock-Induced Developmental Abnormalities

### 1 Heat Shock Effects in Snail Development (With 6 Figures)

ELIDA K. BOON-NIERMEIJER

1 Introduction .....	7
2 Normal Development .....	8
3 Thermosensitivity During Development .....	10
3.1 Terms to Express Thermosensitivity .....	10
3.2 The Cleavage Period: Heat and the Cell Division Cycle .....	11
3.3 Death and Anomalies Induced by Heat During Development of <i>Lymnaea</i> .....	12
3.4 General Implications .....	14
3.4.1 Heat Shock as a Teratogen .....	14
3.4.2 Evidence for a Relationship Between Heat-Induced Anomalies and the Cell Division Cycle .....	16
3.4.3 Hypothesis Concerning Determinative Events .....	17
4 The Heat Shock Response During Development .....	18
4.1 Heat Shock Response and Thermotolerance .....	18
4.2 Definition of Thermotolerance .....	18
4.3 Thermotolerance in <i>Lymnaea</i> : Kinetics and HSP Synthesis .....	19
4.4 Heat-Induced Changes in Thermosensitivity and Gene Expression During Development .....	22
References .....	25

### 2 Environmentally Induced Development Defects in *Drosophila* (With 3 Figures)

NANCY S. PETERSEN and HERSCHEL K. MITCHELL

1 Historical Background .....	29
2 Phenocopy Induction .....	32

2.1	Conditions for Induction of Phenocopies .....	32
2.1.1	Sensitive Periods .....	32
2.1.2	Timing .....	32
2.1.3	Heating Conditions .....	33
2.2	Induction of Phenocopies in Recessive Mutant Heterozygotes .....	33
2.3	Effects of Heat Shock on Gene Expression .....	35
3	Phenocopy Prevention .....	36
3.1	Induction of Phenocopy Thermotolerance .....	36
3.2	Thermotolerance and Heat Shock Proteins .....	36
3.3	Molecular Models for Thermotolerance .....	39
4	Conclusions .....	40
	References .....	41

### 3 The Use of Heat-Shock-Induced Ectopic Expression to Examine the Functions of Genes Regulating Development

GREG GIBSON

1	Scope .....	44
2	The Heat Shock Strategy .....	45
3	Applications .....	47
3.1	Minimal Induction: Sex Determination and Ageing .....	47
3.2	Early Development: Gradients and Metameric Stability .....	48
3.3	Establishing Identity: The Homeotic Genes .....	49
3.3.1	The Functional Structure of Homeotic Proteins .....	49
3.3.2	The Homeotic Regulatory Hierarchy .....	50
3.4	The Fates of Individual Cells: Photoreceptors .....	52
4	Conclusions .....	52
4.1	General Applicability to the Study of Development .....	52
4.2	Prospects .....	54
	References .....	55

### 4 Thermotolerance and Heat Shock Response During Early Development of the Mammalian Embryo (With 7 Figures)

DAVID WALSH, KAREN LI, CAROL CROWTHER, DEBBIE MARSH,  
and MARSHALL EDWARDS

1	Introduction .....	58
2	Developmental Defects Caused by Hyperthermia .....	58
3	The Heat Shock Response in Mammalian Embryos .....	59
3.1	Embryo Culture and Heat Shock Genes .....	60
3.2	Heat Shock and Neural Tube Closure .....	61
3.3	Cell Death of the Neuroectoderm .....	63
3.4	Induction of Heat Shock Proteins .....	63
3.4.1	Translation .....	63
3.4.2	Transcription .....	63

4	Thermotolerance and Heat Shock Protein Synthesis .....	66
5	Heat Shock and Cell Cycle Changes .....	66
6	Conclusion .....	68
	References .....	69

**5 Strain Differences in Expression  
of the Murine Heat Shock Response:  
Implications for Abnormal Neural Development (With 3 Figures)**

MARK D. ENGLE and RICHARD H. FINNELL

1	Introduction .....	71
2	The Heat Shock Proteins .....	71
3	Strain Differences in Heat-Induced Neural Tube Defects .....	72
4	The Murine Heat Shock Response .....	74
4.1	The Heat Shock Response in the Murine Embryo and Lymphocyte .....	74
4.2	A Genetic Basis for Strain Differences in the Murine Heat Shock Response .....	77
4.3	An In Vitro Model of the Murine Heat Shock Response .....	78
5	Conclusions .....	79
	References .....	81

**Part II  
Cell-Specific and Developmental Control  
of Hsp Synthesis**

**6 The Expression of Heat Shock Protein and Cognate Genes  
During Plant Development**

JILL WINTER and RALPH SINIBALDI

1	Introduction .....	85
2	Classes of Heat Stress Proteins and the Putative Functions of the Family Members .....	86
2.1	Hsp104 .....	86
2.2	Hsp90 .....	87
2.3	Hsp70 .....	89
2.4	Hsp60 .....	90
2.5	Low Molecular Weight Hsps (Hsp20 Family) .....	90
2.6	Other Heat Shock Proteins .....	93
3	Hsps and Hscs Expressed During Plant Development .....	93
3.1	Seeds and Seedlings .....	94
3.1.1	Hsps and hsp mRNAs During Seed Development .....	94
3.1.2	Heat Tolerance During Seed Germination and Endogenous Hsps .....	95
3.2	Roots and Leaves .....	96
3.3	Flowering .....	97

3.4	Pollen .....	97
3.4.1	Heat Stress During Pollen Development .....	97
3.4.2	Heat Stress During Pollen Germination .....	98
4	Conclusions .....	100
	References .....	100

**7 Expression of Heat Shock Proteins  
During Development in *Drosophila* (With 3 Figures)**

ANDRÉ P. ARRIGO and ROBERT M. TANGUAY

1	Introduction .....	106
2	Expression of Hsp83 .....	106
3	Expression of Hsp70 and Its Cognates .....	107
4	Expression of the Small Hsps .....	108
4.1	Gene Structure and Control of Expression in the Absence of Stress .....	108
4.2	Tissue-Specific Expression of Hsp27 .....	110
4.3	Tissue-Specific Expression of Hsp26 .....	112
4.4	Tissue-Specific Expression of Hsp23 .....	112
5	Cellular Localization and Function(s) of the Small Hsps During Development .....	113
6	Summary .....	116
	References .....	116

**8 Regulation of Heat Shock Gene Expression  
During *Xenopus* Development (With 12 Figures)**

JOHN J. HEIKKILA, PATRICK H. KRONE, and NICK OVSENEK

1	Introduction .....	120
2	Heat Shock-Induced Accumulation of Hsp and <i>Ubiquitin</i> mRNA in <i>Xenopus</i> Embryos is Developmentally Regulated .....	121
3	Pattern of Hsp and <i>Ubiquitin</i> mRNA Accumulation in Heat Shocked Embryos .....	123
4	Involvement of Cis- and Trans-Acting Factors in the Developmental Regulation of Hsp70 Gene Expression .....	124
5	Regulation of <i>Hsp30</i> Gene Expression During Development .....	131
6	Isolation and Sequence Analysis of <i>Hsp30</i> Genes from a <i>Xenopus laevis</i> Genomic Library .....	133
	References .....	135

## 9 Heat Shock Gene Expression During Mammalian Gametogenesis and Early Embryogenesis

DEBRA J. WOLGEMUTH and CAROL M. GRUPPI

1	Introduction .....	138
1.1	Molecular Approaches to Studying Mammalian Germ-Cell Development .....	138
1.2	Brief Background and Classification of Hsp .....	140
1.3	Significance of Conservation of Coding and Regulatory Regions in <i>hsp</i> Genes .....	141
1.4	Rationale for Examining Hsp Expression and Function in Germ Cells .....	142
2	Heat-Shock Gene Expression and Function During Mammalian Spermatogenesis .....	142
2.1	Key Features of Mammalian Spermatogenesis .....	142
2.2	Expression of the <i>hsp70</i> Gene Family .....	143
2.3	Expression of <i>hsp90</i> Genes .....	144
3	Expression and Function of Hsp During Mammalian Oogenesis and Early Embryogenesis .....	144
3.1	Key Features of Mammalian Oogenesis and Very Early Embryonic Divisions .....	144
3.2	Expression of Hsp in Oocytes and Early Embryos .....	145
4	Summary and Speculation as to Function of Hsp in Mammalian Germ Cells and Embryos .....	146
4.1	Possible Functions of Hsp in General .....	146
4.2	Possible Functions of Heat Shock Genes in Male Germ Cell Differentiation .....	147
4.3	Molecular and Genetic Approaches for Identifying Function During Mammalian Gametogenesis .....	147
References .....		149

## 10 Heat Shock Protein Synthesis in Preimplantation Mouse Embryo and Embryonal Carcinoma Cells (With 3 Figures)

VALÉRIE MEZGER, VINCENT LEGAGNEUX, CHARLES BABINET,  
MICHEL MORANGE, and OLIVER BESNAUDE

1	Introduction .....	153
1.1	The Major Murine Heat-Shock Proteins .....	153
1.2	Heat-Shock Protein Expression During Gametogenesis .....	154
2	Heat-Shock Protein Synthesis in Unstressed Early Embryonic Cells .....	155
2.1	Heat-Shock Proteins, the First Major Products of Zygotic Transcription .....	155
2.2	High Spontaneous Expression of Hsps in the Preimplantation Mouse Embryo .....	156
2.3	Hsp Expression in Embryonal Carcinoma Cells .....	156
3	Transcription of Heat Shock Genes in Unstressed EC Cells .....	157
3.1	Transcriptional and Posttranscriptional Regulation of Spontaneous Hsp Synthesis in EC Cells .....	157

3.2	HSE-Binding Activity in EC Cells .....	157
3.3	An Ela-Like Activity in EC Cells .....	158
3.4	High Levels of B2 Transcripts in Undifferentiated Mouse Embryonic Cells .....	159
4	Defective Heat Shock Response in Early Embryonic Cells .....	160
4.1	Lack of Heat Shock Protein Inducibility in the Early Preimplantation Mouse Embryo .....	160
4.2	Inducible and Noninducible Embryonal Cell Lines .....	160
4.3	Noninducible EC Cells are Deficient in Transcriptional Transactivation of Heat Shock Genes by Stress .....	162
4.4	HSE-Binding Activity in Heat-Shocked EC Cells .....	163
5	Concluding Remarks .....	163
	References .....	164

**11 Transcriptional Regulation of Human *Hsp70* Genes:  
Relationship Between Cell Growth, Differentiation,  
Virus Infection, and the Stress Response (With 5 Figures)**

BENETTE PHILLIPS and RICHARD I. MORIMOTO

1	Introduction .....	167
2.	Factors Which Alter the Expression of <i>Hsp70</i> , <i>Grp78</i> , and <i>P72</i> .....	168
2.1	Factors Which Alter Expression of <i>Hsp70</i> .....	168
2.1.1	Determinants of Basal Expression .....	168
2.1.2	Classical Stress-Response Inducers .....	170
2.1.3	DNA Viruses .....	170
2.1.4	Cell Cycle Regulation, Growth Factors .....	173
2.1.5	Agents Inducing Differentiation .....	173
2.1.6	Other Agents .....	175
2.2	Factors Which Alter the Expression of <i>Grp78</i> .....	175
2.3	Factors Which Alter the Expression of <i>P72</i> .....	176
3	Mechanisms of Activation .....	176
3.1	Heat Shock Induction .....	177
3.2	Hemin Induction .....	180
3.3	Viral Induction .....	182
3.3.1	Adenovirus .....	182
3.3.2	Herpes Simplex Virus-1 (HSV-1) .....	183
3.3.3	Simian Virus 5 (SV5) .....	183
4	Concluding Remarks .....	184
	References .....	184

**12 Transforming Growth Factor- $\beta$   
Regulates Basal Expression of the *hsp70* Gene Family  
in Cultured Chicken Embryo Cells (With 5 Figures)**

IVONE M. TAKENAKA, SETH SADIS, and LAWRENCE E. HIGHTOWER

1	Introduction .....	188
2	Biochemical and Biological Properties of TGF- $\beta$ .....	189
3	TGF- $\beta$ in Embryogenesis and Development .....	191
4	Heat Shock Proteins Are Induced During Embryogenesis and in Highly Mitogenic Cells .....	192
5	Regulators of Basal Expression of Heat Shock Gene Families in Unstressed Cells .....	194
6	TGF- $\beta$ Rapidly Induces Hsc70 in Cultured Chicken Embryo Cells .....	195
7	The Hsc70 Molecular Chaperone Interacts with Diverse Polypeptide Sequences .....	200
8	Conclusion .....	204
References .....		205

**13 Cell Growth, Cytoskeleton, and Heat Shock Proteins (With 2 Figures)**

ICHIRO YAHARA, SHIGEO KOYASU, KAZUKO IIDA, HIDETOSHI IIDA,  
FUMIO MATSUZAKI, SEIJI MATSUMOTO, and YOSHIHIKO MIYATA

1	Cyclic AMP and Expression of Heat Shock Proteins in the Budding Yeast .....	210
2	Heat Shock-Induced Reorganization of Cytoskeletal Structures .....	211
3	Hsp90 is an Actin-Binding Protein .....	213
References .....		215

**14 Expression of Heat Shock Genes (*hsp70*)  
in the Mammalian Nervous System (With 4 Figures)**

IAN R. BROWN

1	Introduction .....	217
2	Early Studies on Brain Heat-Shock Proteins .....	218
3	Induction of Heat Shock Proteins in the Visual System .....	218
4	Analysis of <i>hsp70</i> mRNAs in the Mammalian Nervous System .....	219
5	Regional Differences in Expression of <i>hsp70</i> Genes in Brain Detected by In Situ Hybridization .....	219
6	Induction of an Hsp70 Gene at the Site of Tissue Injury in the Brain .....	222
7	Immunological Detection of Hsp70 in Brain Tissue .....	224
8	Tissue-Protective Effects of Heat Shock in the Nervous System .....	225
9	Conclusion .....	226
References .....		226