

Contents

1 Introduction – Morphology of the Liver Lobule 1

PART I

Cells of the Liver Lobule 7

2 Hepatocytes 9

2.1 Morphology of Parenchymal Liver Cells 10

2.2 Functions of Hepatocytes 10

2.3 Heterogeneity of Hepatocytes and Nonparenchymal Liver Cells Inside the Liver Lobule 11

3 Sinusoidal Endothelial Cells 13

3.1 Morphology 13

3.2 Cellular Functions 14

3.2.1 Filtration 14

3.2.2 Endocytosis, Pinocytosis, Phagocytosis, and Transcytosis 14

3.2.3 Immunological Function 17

3.2.4 Secretory Activity 18

3.2.5 Other Functions 18

4 Kupffer Cells 21

4.1 Morphology 21

4.2 Distribution and Origin 22

4.3 Isolation 23

4.4 Activation of Kupffer Cells 23

4.5 Functions 26

5 Hepatic Stellate Cells 29

5.1 Morphology of Stellate Cells in Liver Sections 29

5.2 Isolation 31

5.3 Morphology and Functions of Stellate Cells in Early Cultures 31

5.4 Morphology and Functions of Activated Hepatic Stellate Cells 32

5.4.1 Activation of Hepatic Stellate Cells 32

5.4.2 Functions 34

5.4.3	Receptors and Secretory Products	35
5.5	Heterogeneity of Hepatic Stellate Cells and Liver Myofibroblasts	36
5.6	Differences Between Human and Rat Hepatic Stellate Cells	39
6	Pit Cells and Other Intrahepatic Lymphocytes	41
6.1	Isolation	41
6.2	Phenotype of Intrahepatic Lymphocyte Populations .	42
6.3	Origin and Development of Pit Cells	43
6.4	Morphology of Pit Cells	44
6.5	Functions of Pit Cells	45

PART II

Cross-Talk of Liver Cells in Physiology and Pathology . . . 47

7	Cooperation of Liver Cells in the Synthesis and Degradation of Eicosanoids	51
7.1	Synthesis and Catabolism of Eicosanoids	51
7.2	Cellular Sources of Eicosanoids in the Liver	53
7.3	Expression of Prostanoid Receptors	54
	on Different Types of Liver Cells	54
7.4	Functions of Eicosanoids in the Liver	57
7.4.1	Prostaglandins	57
7.4.2	Leukotrienes	58
8	Nitric Oxide as a Mediator of Intercellular Communication in the Liver	61
8.1	Nitric Oxide Synthesis in Liver Cells	
8.1.1	Regulation of NO Synthesis in Hepatocytes .	61
8.1.2	Regulation of NO Synthesis in Kupffer Cells .	62
8.1.3	Regulation of NO Synthesis in Sinusoidal Endothelial Cells and Hepatic Stellate Cells	63
8.2	Nitric Oxide Effects on Liver Function	64
9	Cooperation of Hepatocytes and Stellate Cells in the Metabolism and Storage of Retinoids	65
10	Cooperation of Liver Cells in the Regulation of Glucose Metabolism	69
10.1	Effects of Prostaglandins	69
10.2	Effects of Cytokines and Nitric Oxide	72
11	Cooperation of Liver Cells in the Synthesis of Growth Factors and Respective Binding Proteins .	73
11.1	Insulin-Like Growth Factors and IGF-Binding Proteins	73

11.2	Role of Hepatocyte Growth Factor in the Communication Between Hepatocytes and Stellate Cells	75
11.3	Cross-Talk of Liver Cells in the Synthesis of TGF- β and TGF- β -Binding Proteins	76
12	Cooperation of Liver Cells in the Regulation of Sinusoidal Contractility	79
13	Cross-Talk of Liver Cells in Response to Endotoxin . .	83
13.1	Endotoxin Uptake by the Liver	83
13.2	Activation of Nonparenchymal Liver Cells as the Early Response to Endotoxin	84
13.2.1	TNF- α as a Paracrine Mediator in Liver Responses to Endotoxin	86
13.2.2	The Role of Nitric Oxide in the Response of Liver Cells to Endotoxin	88
13.3	The Interactions of Neutrophils with Liver Cells in Endotoxemia	89
13.4	Interactions of Liver Cells in the Production and Removal of Reactive Oxygen Species	92
13.5	Cross-Talk of Liver Cells in Endotoxin-Induced Metabolic Alterations	94
13.5.1	Interactions of Liver Cells During the Synthesis of Acute-Phase Proteins	94
13.5.2	Cooperation of Liver Cells in the Regulation of Glucose Metabolism in Endotoxemia	95
14	Cooperation of Liver Cells in the Process of Liver Fibrosis	97
14.1	Factors Involved in the Activation of Hepatic Stellate Cells	97
14.2	Cellular Cross-Talk During Activation of Stellate Cells and Progression of Hepatic Fibrogenesis	100
14.3	Factors Influencing the Resolution of Initial Fibrotic Changes of the Liver	104
15	Perspectives	107
16	Summary	109
	References	115
	Subject Index	149