

Hepatobiliary Transport in Health and Disease

Bearbeitet von
Dieter Häussinger, Verena Keitel, Ralf Kubitz

1. Auflage 2012. Buch. XX, 292 S. Hardcover

ISBN 978 3 11 027899 6

Format (B x L): 17 x 24 cm

Gewicht: 721 g

[Weitere Fachgebiete > Medizin > Klinische und Innere Medizin > Hepatologie](#)

schnell und portofrei erhältlich bei

The logo for beck-shop.de features the text 'beck-shop.de' in a bold, red, sans-serif font. Above the 'i' in 'shop' are three red dots of increasing size. Below the main text, the words 'DIE FACHBUCHHANDLUNG' are written in a smaller, red, all-caps, sans-serif font.

beck-shop.de
DIE FACHBUCHHANDLUNG

Die Online-Fachbuchhandlung [beck-shop.de](#) ist spezialisiert auf Fachbücher, insbesondere Recht, Steuern und Wirtschaft. Im Sortiment finden Sie alle Medien (Bücher, Zeitschriften, CDs, eBooks, etc.) aller Verlage. Ergänzt wird das Programm durch Services wie Neuerscheinungsdienst oder Zusammenstellungen von Büchern zu Sonderpreisen. Der Shop führt mehr als 8 Millionen Produkte.

Contents

Preface	v
List of Contributors	vii
Abbreviations	xvii

1 Physiology of bile formation: Hepatocellular

bile salt transporters	1
1.1 Introduction	1
1.2 Sodium-dependent bile salt uptake into hepatocytes	3
1.3 Sodium-independent bile salt uptake into hepatocytes	7
1.4 Bile salt export across the canalicular membrane	8
1.5 Bile salt salvage systems	12
1.6 Concluding remarks	12
1.7 References	13

2 Structure and function of hepatic ABC transporters

2.1 Introduction to human ABC transporters expressed in the liver	23
2.2 Structure and function of the bile salt export pump (ABCB11; BSEP)	25
2.3 Structure and function of the multidrug resistance protein 3 (ABCB4; MDR3)	32
2.4 Structure and function of the breast cancer resistance protein (ABCG2; BCRP)	37
2.5 Concluding remarks	40
2.6 References	41

3 Short- and long-term regulation of hepatobiliary transport

3.1 Introduction	49
3.2 Short-term regulation of sinusoidal transport systems	49
3.3 Long-term regulation of sinusoidal transport systems	51
3.4 Short-term regulation of canalicular secretion	54
3.5 Long-term regulation of canalicular transport systems	56
3.6 Methods of studying subcellular transporter distribution	58
3.7 Summary	59
3.8 References	60

4 Nuclear bile acid receptor FXR

and hepatobiliary transport systems	71
4.1 Introduction	71
4.2 Nuclear receptors	71
4.3 Bile acids and the enterohepatic circulation	74
4.4 Bile acid homeostasis, enterohepatic circulation, and FXR	75
4.5 The role of FXR in the pathogenesis of biliary diseases	79

4.6	Concluding remarks	80
4.7	References.....	81
5	Bile acid signaling in the liver and the biliary tree	85
5.1	Introduction.....	85
5.2	Bile acid signaling in liver parenchymal cells (hepatocytes)	85
5.3	Bile acid signaling in sinusoidal endothelial cells	89
5.4	Bile acid signaling in Kupffer cells	90
5.5	Bile acid signaling in hepatic stellate cells	91
5.6	Bile acid signaling in the biliary tree	93
5.7	References.....	96
6	Modulation of innate immunity and inflammation by bile acids and their receptors.....	103
6.1	Introduction.....	103
6.2	Impact of FXR deletion on immunity and inflammation – lessons from FXR knockout mice	106
6.3	Role of TGR5 in the modulation of immune function.....	108
6.4	Effects of bile acids on immunological function independently of bile acid receptors.....	109
6.5	Obstructive jaundice and its impact on immune function	110
6.6	Role of bile acids and FXR in viral infections	111
6.7	Concluding remarks	111
6.8	References.....	112
7	Bile acids as extrahepatic and interorgan signaling molecules	117
7.1	Introduction.....	117
7.2	Bile acid–dependent modulation of glucose homeostasis	118
7.3	Impact of bile acids on energy expenditure	120
7.4	Bile acid receptors and immune response.....	120
7.5	Role of bile acid receptors in the cardiovascular system	121
7.6	Role of bile acid receptors in the kidney	122
7.7	Bile acid receptors in the central and peripheral nervous system	124
7.8	Summary and future perspectives	124
7.9	References.....	125
8	Disorders of bile duct development.....	131
8.1	Introduction.....	131
8.2	Morphogenesis of the intrahepatic bile duct epithelium: molecular players involved and their relationship with arterial morphogenesis.....	131
8.3	Ductal plate malformation (DPM): definition, clinical heterogeneity, and classification based on animal models	136
8.4	Cilia in cholangiocytes: a multifunctional transducing system.....	136
8.5	DPM-related cholangiopathies	138
8.6	Alagille's syndrome (AGS)	145
8.7	References.....	146

9 Mutations of the bile salt export pump (BSEP) and multidrug-resistance protein 3 (MDR3)	151
9.1 Introduction	151
9.2 BSEP-related liver diseases	151
9.3 MDR3-related liver diseases	158
9.4 Treatment of BSEP- and MDR3-associated liver diseases	162
9.5 Concluding remarks	162
9.6 References	163
10 MRP2 (ABCC2) and disorders of bilirubin handling in liver	171
10.1 Introduction	171
10.2 The conjugate efflux pump MRP2 in the hepatocyte canalicular membrane	171
10.3 Formation of unconjugated bilirubin and its uptake into hepatocytes	173
10.4 Formation of bilirubin glucuronides and their transport into bile by MRP2	174
10.5 Uptake of bilirubin glucuronides into hepatocytes	174
10.6 MRP3, a basolateral efflux pump, contributes to conjugated hyperbilirubinemia	175
10.7 Genetic disorders and drug-induced inhibition of bilirubin uptake into hepatocytes	175
10.8 Genetic variants of the <i>MRP2 (ABCC2)</i> gene and MRP2 deficiency in Dubin-Johnson syndrome	176
10.9 Impairment of MRP2 localization in the hepatocyte canalicular membrane	177
10.10 References	177
11 Hepatobiliary transport during pregnancy: Cross talk between transporters and hormones	183
11.1 Introduction	183
11.2 Estrogens as cholestatic agents	183
11.3 Cholestatic activity of progesterone	185
11.4 Biochemical observations in symptom-free pregnant women	186
11.5 Genetic lessons from congenital cholestasis	186
11.6 Transporter variants and cholestasis of pregnancy	187
11.7 Nuclear receptors and cholestasis of pregnancy	189
11.8 Gallstones and pregnancy	189
11.9 Concluding remarks	190
11.10 References	190
12 Hepatobiliary transport and gallstone formation	195
12.1 Introduction	195
12.2 Epidemiology and risk factors of cholelithiasis	195
12.3 Hepatobiliary transporters and the pathophysiology of gallstone formation	196

12.4	Genetic variation in hepatobiliary transporter genes and gallstone susceptibility	199
12.5	Concluding remarks	202
12.6	References.....	203
13	Molecular basis of primary biliary cirrhosis	207
13.1	Introduction	207
13.2	Pathogenesis of PBC	210
13.3	Concluding remarks	214
13.4	References.....	215
14	The molecular basis of primary sclerosing cholangitis	223
14.1	Introduction	223
14.2	Immune-mediated bile duct injury	227
14.3	Toxic bile duct injury	231
14.4	Fibrosis and cirrhosis	232
14.5	Cancer development	233
14.6	Concluding remarks	233
14.7	References.....	235
15	Drug-induced cholestatic liver injury	241
15.1	Introduction	241
15.2	Diagnostic criteria of drug-induced cholestasis.....	241
15.3	Hepatocellular drug concentration	242
15.4	Hepatic bile salt accumulation	244
15.5	Susceptibility to drug-induced cholestasis	245
15.6	Concluding remarks	247
15.7	References.....	247
16	Bile acids and receptors: Therapeutic relevance	253
16.1	Introduction	253
16.2	Nuclear and membrane BA receptors: general concepts.....	253
16.3	Therapeutic potential of BAs	254
16.4	Role of BA receptors in BA homeostasis and bile production: therapeutic implications in cholestasis.....	254
16.5	Role of BA receptors for targeting hepatic inflammation and fibrosis	257
16.6	Role of BA receptors in the pathogenesis and treatment of gallstone disease	258
16.7	BA receptors in intestine: therapeutic implications for the gut-liver axis and inflammatory bowel disease.....	259
16.8	Role of BAs in lipid metabolism: therapeutic implications for atherosclerosis and nonalcoholic fatty liver disease (NAFLD)	260
16.9	Role of BAs in hepatic glucose metabolism and beyond	262
16.10	BA receptors in hepatobiliary and colorectal cancer.....	264
16.11	BA receptors beyond the liver and gastrointestinal tract.....	265

16.12	Concluding remarks	265
16.13	References	266
17	Analysis of bile acids by tandem mass spectrometry.....	277
17.1	Introduction	277
17.2	Experimental procedures	278
17.3	Applications	281
17.4	Summary	286
17.5	References.....	287
Index		289