Supplementary Table S1. Most commonly used animal models for the study of liver diseases. Strength, Limitations and translatability to clinical studies.

Liver Disease	Animal Models	Strength	Limitations	Translatability to clinical studies	References
ALD	**A-DW model**	Easy to perform Mild steatosis Short- or long-term feeding	No liver fibrosis Natural aversion in rodent	ALD animal models fail to replicate the all-round spectrum of human pathology ALD rodent model would address: ethanol metabolism, oxidative stress presence, ROS production and immune system activation	[1–8]
	LDC model	Easy to perform Steatosis Short term feeding with no mortality rate	Mild mortality No liver fibrosis Low-level inflammation		
	NIAAA model	Cost and time efficient High blood alcohol levels Easy to perform Steatosis Liver injury Inflammation	High mortality No liver fibrosis Represent only early alcoholic steatohepatitis		
	LDC + "second hit" (LDC+CCl_4, LDC+DEN, LDC+ LPS, LDC+APAP)	Easy to perform Marked elevation of ALT and marked steatosis Steatosis Liver fibrosis	High mortality Toxic components		
NAFLD	**Dietary models (HFD, HF-HC, MCD)**	Animals develop histologic and metabolic features of human NASH at 2-4 weeks	Lose weight Diffuse fibrosis No cirrhosis	Difference with human diet Patients with NASH are not choline-deficient	[6,9–23]
	Genetic models (ob/ob, fa/fa, SREBP-1c transgenic)	Steatosis Insulin resistance Obesity	Modest fibrosis ~ 24 weeks to develop steatohepatitis without other insult Severe and expensive	Metabolic and transcriptomic features in the liver are not totally in concordance to human NASH	
	Combination therapies using chemicals (WD+CCl_4)	Progressive steatosis Insulin resistance Fibrosis at 12 weeks Cirrhosis HCC at 24 weeks	Not represent human environment Potential health hazards for its investigator		

Liver Disease	Animal Models	Strength	Limitations	Translatability	References
HCC	**Transplantation-based models (Xenograft, Isograft)**	Use of immune-deficient mice to avoid rejections	Cell-line derived xenografts lack the typical tumor cell heterogeneity Unnatural environment for tumor growth	Immunological barrier produce rejections Impossibility to study the immune system in tumor development	[4,6,19,24–28]
	Chemically-induced models) DEN	Mimic the carcinogenesis produced from hepatotoxic compounds	Hepatotoxins produce particular liver lesions Poorly reproducible Slow tumor formation Metastases are not observed	Reproduce the typical damage and episodes in the human cancer	
	Combination therapies (DEN+CCL_4, WD+CCl_4)	Obesity and simple steatosis in DEN+ CCL_4 model Fibrosis by 12 weeks and HCC by 24 weeks in WD+CCl_4 model	Potential health hazards for its investigator	Hepatic transcriptomic alignment with human NASH	
Portal hypertension	**Partial portal vein ligation (PPVL)**	Easy surgery Low mortality Inexpensive Reproducible High PP after 2 days Portal-systemic shunting and hyperdynamic circulatory changes	No fibrosis No cirrhosis	Not all models express all disturbances characteristic of the portal hypertension syndrome	[17,29–33]
	BDL	Reproducible Secondary biliary fibrosis and cirrhosis in 4–6 weeks Periportal fibrosis after 1-3 weeks 50% ascites	10% Mortality rate in the first week High mortality 7-10 weeks after induction Not suitable for pharmacological studies with drugs that are eliminated through the biliary route Mice develop marked dilation of the gallbladder after bile duct ligation, which may lead to perforation and choleperitoneum due to the presence of gallbladder		
	CCl_4	Histological changes in centrolobular area by 4 weeks Progressive increase in PP in parallel with fibrosis Cirrhosis at week 16	Potential health hazards for its investigator Differences in development of PH due to different sensitivity to CCl_4 Peritoneal injection may cause damage in peritoneum, liver and intestines		
Liver Disease	**Animal Models**	**Strength**	**Limitations**	**Translatability**	**References**

Angiogenesis	**Genetic models (retroviral, lentiviral, sh/siRNA knock-down, CRISPR/Cas9-based method)**	Efficient and practical knock-out of genes	Time consuming Expensive Requires careful genotyping	Angiogenesis is only a therapeutic target for liver fibrosis	[34–37]

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