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Supplementary Table 1. Selection of host-directed therapies for chronic HBV, HCV and HIV infections.

Infection	Strategy	Agent	Status of development	Ref
Chronic hepatitis B	Blocking virus entry by targeting NTCP	myrcludex B (peptide derived from HBV large surface glycoprotein)	Phase Ib/IIa study of patients with chronic HBV – HDV co-infection; orphan drug status by the EMA and the FDA	1,2
	Enhancing the immune response by treatment with IFN-α	Peg-conjugated IFNα-2a (Pegasys); IFNα-2b (Intron A)	PegIFNα-2a for treatment of adult patients with HBeAg positive or negative chronic hepatitis B, compensated liver disease, liver inflammation and evidence of viral replication; Intron A for chronic hepatitis B in patients 1 year of age or older with compensated liver disease	3-7
	Therapeutic vaccination to enhance cellular immunity and cell-based immunotherapy	HBsAg complexed with HBIG	Phase IIb trial: HBsAg seroconversion only in group with highest vaccine dose, but not statistically significant	8
		Multi-epitope vaccines; combination of vaccine with immune check point inhibitors; protein-prime MVA-boost vaccination	Preclinical stages	9,10
		DNA-based genetic vaccines (with	Proof-of-concept study	11,12

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		nucleoside analogue)		
		CAR-redirected T cells	Preclinical development	13
Chronic hepatitis C	Enhancing the immune response by treatment with IFNs	IFN alfacon-1 (Infergen); IFNα-2b (Intron A); IFNα-2a (Roferon); Peg-conjugated IFNα-2a (Pegasys); PegIFNα-2b (PegIntron); PegIFN-λ1a	Approved IFN-α types and formulations, often in combination with ribavirin; PegIFN-λ1a: phase IIb study	14,15
	Inhibiting viral replication by sequestering cyclophilin A (CypA)	Non-immunosuppresive derivates of cyclosporine A (CsA) such as alisporivir, NIM811, SCY-635	Clinical studies of alisporivir with a total patient population of ~1.800 patients; exploratory phase II and 2 trials for SCY-635 and NIM811; no further clinical studies due to the success of DAAs	16,17 18-20
	Inhibiting viral replication by sequestering cellular miR-122	Antagomirs: antisense oligonucleotides to miR-122	Preclinical studies with knock-out mice revealed tumor suppressor function for miR-122; only one clinical candidate in further development	21-23
HIV-1	Blocking virus entry by antagonizing the co-receptor CCR5; additional immunological benefit by	Maraviroc (Selzentry® or Celsentri®)	Approved	24

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	increasing the levels of CD4+ and CD8+ T cells			
	Enhancing immune response by treatment with IFNs	PegIFNα-2a	Phase II clinical trial of HIV-1 monoinfected patients	25
	Eliminate reactivated cells in the latent HIV reservoir	Acitretin (retinoic acid derivate)	*Ex vivo* studies	26
	Cell-based immunotherapy	CAR-redirected T cells: e.g. CD4ζ	Phase II randomized study; preclinical study of CAR-engrafted T-cells co-expressing shRNAs targeting CCR5 and the HIV-1 genome	27-33
	Therapeutic vaccines	Serial immunization with MVA and Fowlpox virus expressing multiple HIV-1 genes	Phase I clinical trial in young adults on effective HAART	34

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