SUPPLEMENTARY MATERIAL AND METHODS

Fluorescent antibodies

The following fluorochrome labeled antibodies were used for surface and intracellular staining: Anti-CD107a (H4A3), anti-CD14 (M5E2), anti-CD19 (HIB19), anti-CD25 (M-A251), anti-CD3 (SK7), anti-CD4RPA-T4, anti-CD45RA (HI100), anti-CD56 (NCAM16.2), anti-CD8 (RPA-T8), anti-FoxP3 (259D/C7), anti-gdTCR (B1), anti-Granzyme B (GB11), anti-CD14 (MφP9), anti-CD19 (HIB19), anti-PD-1 (EH12.1), anti-CD14 (M5E2), anti-CD19 (SJ24C1), anti- IFN-γ (B27) and anti-MIP-1β (D21-1351) from BD Biosciences; anti-CCR7 (G043H7), anti-CD11c (Bu15), anti-CD127 (A019D5), anti-CD14 (63D3), anti-CD141 (M80), anti-CD16 (5C8), anti-CD1c (L161), anti-CD3 (UCHT1), anti-CD303 (201A), anti-CD39 (A1), anti-CD8 (RPA-T8), anti-CD86 (IT2.2), anti-HLA-DR (L243), anti-HLA-DR, anti-Ki-67 (Ki-67), anti-PD-1 (EH12.2H7), anti-Tbet (4B10), anti-TCF-1 (7F11A10), anti-TCR Vα7.2 (3C10) and anti-TNF-α (Mab11) from Biolegend (San Diego, CA, USA); anti-CD154 (5C8) and anti-KLRG1 (REA261) from Miltenyi Biotec; and anti-Eomes (WD1928) from Thermo Fisher Scientific.

SUPPLEMENTARY TABLES

Supplementary Table 1. Overlapping peptides of HBV genotype D and amino acid sequences

Core antigen:

Peptide pool	Peptide number	Amino acid sequence
Core pool 1	Peptide 1	[H]MQLFHLCLIISCSCP[OH]
	Peptide 2	[H]LCLIISCSCPTVQAS[OH]
	Peptide 3	[H]SCSCPTVQASKLCLG[OH]
	Peptide 4	[H]TVQASKLCLGWLWGM[OH]
	Peptide 5	[H]KLCLGWLWGMDIDPY[OH]
	Peptide 6	[H]WLWGMDIDPYKEFGA[OH]
	Peptide 7	[H]DIDPYKEFGATVELL[OH]
	Peptide 8	[H]KEFGATVELLSFLPS[OH]
	Peptide 9	[H]TVELLSFLPSDFFPS[OH]
	Peptide 10	[H]SFLPSDFFPSVRDLL[OH]
	Peptide 11	[H]DFFPSVRDLLDTASA[OH]
	Peptide 12	[H]VRDLLDTASALYREA[OH]
	Peptide 13	[H]DTASALYREALESPE[OH]
	Peptide 14	[H]LYREALESPEHCSPH[OH]
	Peptide 15	[H]LESPEHCSPHHTALR[OH]
	Peptide 16	[H]HCSPHHTALRQAILC[OH]
	Peptide 17	[H]HTALRQAILCWGELM[OH]
	Peptide 18	[H]QAILCWGELMTLATW[OH]
	Peptide 19	[H]WGELMTLATWVGVNL[OH]
	Peptide 20	[H]TLATWVGVNLEDPAS[OH]
Core pool 2	Peptide 21	[H]VGVNLEDPASRDLVV[OH]
	Peptide 22	[H]EDPASRDLVVSYVNT[OH]
	Peptide 23	[H]RDLVVSYVNTNMGLK[OH]
	Peptide 24	[H]SYVNTNMGLKFRQLL[OH]
	Peptide 25	[H]NMGLKFRQLLWFHIS[OH]
	Peptide 26	[H]FRQLLWFHISCLTFG[OH]
	Peptide 27	[H]WFHISCLTFGRETVI[OH]
	Peptide 28	[H]CLTFGRETVIEYLVS[OH]
	Peptide 29	[H]RETVIEYLVSFGVWI[OH]
	Peptide 30	[H]EYLVSFGVWIRTPPA[OH]
	Peptide 31	[H]FGVWIRTPPAYRPPN[OH]
	Peptide 32	[H]RTPPAYRPPNAPILS[OH]
	Peptide 33	[H]YRPPNAPILSTLPET[OH]

	Peptide 34	[H]APILSTLPETTVVRR[OH]
	Peptide 35	[H]TLPETTVVRRRGRSP[OH]
	Peptide 36	[H]TVVRRRGRSPRRRTP[OH]
	Peptide 37	[H]RGRSPRRRTPSPRRR[OH]
	Peptide 38	[H]RRRTPSPRRRRSQSP[OH]
	Peptide 39	[H]SPRRRRSQSPRRRRS[OH]
	Peptide 40	[H]RSQSPRRRRSQSREP[OH]
	Peptide 41	[H]QSPRRRRSQSREPQC[OH]

Surface antigen:

Peptide pool	Peptide number	Amino acid sequence
Surface pool 1	Peptide 1	[H]MGQNLSTSNPLGFFP[OH]
	Peptide 2	[H]STSNPLGFFPDHQLD[OH]
	Peptide 3	[H]LGFFPDHQLDPAFRA[OH]
	Peptide 4	[H]DHQLDPAFRANTANP[OH]
	Peptide 5	[H]PAFRANTANPDWDFN[OH]
	Peptide 6	[H]NTANPDWDFNPNKDT[OH]
	Peptide 7	[H]DWDFNPNKDTWPDAN[OH]
	Peptide 8	[H]PNKDTWPDANKVGAG[OH]
	Peptide 9	[H]WPDANKVGAGAFGLG[OH]
	Peptide 10	[H]KVGAGAFGLGFTPPH[OH]
	Peptide 11	[H]AFGLGFTPPHGGLLG[OH]
	Peptide 12	[H]FTPPHGGLLGWSPQA[OH]
	Peptide 13	[H]GGLLGWSPQAQGILQ[OH]
	Peptide 14	[H]WSPQAQGILQTLPAN[OH]
	Peptide 15	[H]QGILQTLPANPPPAS[OH]
	Peptide 16	[H]TLPANPPPASTNRQT[OH]
	Peptide 17	[H]PPPASTNRQTGRQPT[OH]
	Peptide 18	[H]TNRQTGRQPTPLSPP[OH]
	Peptide 19	[H]GRQPTPLSPPLRNTH[OH]
Surface pool 2	Peptide20	[H]PLSPPLRNTHPQAMQ[OH]
	Peptide21	[H]LRNTHPQAMQWNSTT[OH]
	Peptide22	[H]PQAMQWNSTTFHQTL[OH]
	Peptide23	[H]WNSTTFHQTLQDPRV[OH]
	Peptide24	[H]FHQTLQDPRVRGLYF[OH]
	Peptide25	[H]QDPRVRGLYFPAGGS[OH]
	Peptide26	[H]RGLYFPAGGSSSGAV[OH]
	Peptide27	[H]PAGGSSSGAVNPVPT[OH]
	Peptide28	[H]SSGAVNPVPTTASPL[OH]
	Peptide29	[H]NPVPTTASPLSSIFS[OH]

	Peptide30	[H]TASPLSSIFSRIGDP[OH]
	Peptide31	[H]SSIFSRIGDPALNME[OH]
	Peptide32	[H]RIGDPALNMENITSG[OH]
	Peptide33	[H]ALNMENITSGFLGPL[OH]
	Peptide34	[H]NITSGFLGPLLVLQA[OH]
	Peptide35	[H]FLGPLLVLQAGFFLL[OH]
	Peptide36	[H]LVLQAGFFLLTRILT[OH]
	Peptide37	[H]GFFLLTRILTIPQSL[OH]
	Peptide38	[H]TRILTIPQSLDSWWT[OH]
Surface pool 3	Peptide 39	[H]IPQSLDSWWTSLNFL[OH]
	Peptide 40	[H]DSWWTSLNFLGGTTV[OH]
	Peptide 41	[H]SLNFLGGTTVCLGQN[OH]
	Peptide 42	[H]GGTTVCLGQNSQSPT[OH]
	Peptide 43	[H]CLGQNSQSPTSNHSP[OH]
	Peptide 44	[H]SQSPTSNHSPTSCPP[OH]
	Peptide 45	[H]SNHSPTSCPPTCPGY[OH]
	Peptide 46	[H]TSCPPTCPGYRWMCL[OH]
	Peptide 47	[H]TCPGYRWMCLRRFII[OH]
	Peptide 48	[H]RWMCLRRFIIFLFIL[OH]
	Peptide 49	[H]RRFIIFLFILLLCLI[OH]
	Peptide 50	[H]FLFILLLCLIFLLVL[OH]
	Peptide 51	[H]LLCLIFLLVLLDYQG[OH]
	Peptide 52	[H]FLLVLLDYQGMLPVC[OH]
	Peptide 53	[H]LDYQGMLPVCPLIPG[OH]
	Peptide 54	[H]MLPVCPLIPGSSTTS[OH]
	Peptide 55	[H]PLIPGSSTTSTGPCR[OH]
	Peptide 56	[H]SSTTSTGPCRTCMTT[OH]
	Peptide 57	[H]TGPCRTCMTTAQGTS[OH]
Surface pool 4	Peptide 58	[H]TCMTTAQGTSMYPSC[OH]
	Peptide 59	[H]AQGTSMYPSCCCTKP[OH]
	Peptide 60	[H]MYPSCCCTKPSDGNC[OH]
	Peptide 61	[H]CCTKPSDGNCTCIPI[OH]
	Peptide 62	[H]SDGNCTCIPIPSSWA[OH]
	Peptide 63	[H]TCIPIPSSWAFGKFL[OH]
	Peptide 64	[H]PSSWAFGKFLWEWAS[OH]
	Peptide 65	[H]FGKFLWEWASARFSW[OH]
	Peptide 66	[H]WEWASARFSWLSLLV[OH]
	Peptide 67	[H]ARFSWLSLLVPFVQW[OH]
	Peptide 68	[H]LSLLVPFVQWFVGLS[OH]
	Peptide 69	[H]PFVQWFVGLSPTVWL[OH]
	Peptide 70	[H]FVGLSPTVWLSVIWM[OH]
	Peptide 71	[H]PTVWLSVIWMMWYWG[OH]
	Peptide 72	[H]SVIWMMWYWGPSLYS[OH]

	Peptide 73	[H]MWYWGPSLYSILSPF[OH]
	Peptide 74	[H]PSLYSILSPFLPLLP[OH]
	Peptide 75	[H]ILSPFLPLLPIFFCL[OH]
	Peptide 76	[H]FLPLLPIFFCLWVYI[OH]

Polymerase antigen:

Peptide pool	Peptide number	Amino acid sequence
Polymerase pool 1	Peptide 1	[H]MPLSYQHFRKLLLLD[OH]
	Peptide 2	[H]QHFRKLLLLDDEAGP[OH]
	Peptide 3	[H]LLLLDDEAGPLEEEL[OH]
	Peptide 4	[H]DEAGPLEEELPRLAD[OH]
	Peptide 5	[H]LEEELPRLADEGLNR[OH]
	Peptide 6	[H]PRLADEGLNRRVAED[OH]
	Peptide 7	[H]EGLNRRVAEDLNLGN[OH]
	Peptide 8	[H]RVAEDLNLGNLNVSI[OH]
	Peptide 9	[H]LNLGNLNVSIPWTHK[OH]
	Peptide 10	[H]LNVSIPWTHKVGNFT[OH]
	Peptide 11	[H]PWTHKVGNFTGLYSS[OH]
	Peptide 12	[H]VGNFTGLYSSTVPVF[OH]
	Peptide 13	[H]GLYSSTVPVFNPHWK[OH]
	Peptide 14	[H]TVPVFNPHWKTPSFP[OH]
	Peptide 15	[H]NPHWKTPSFPNIHLH[OH]
	Peptide 16	[H]TPSFPNIHLHQDIIK[OH]
	Peptide 17	[H]NIHLHQDIIKKCEQF[OH]
	Peptide 18	[H]QDIIKKCEQFVGPLT[OH]
	Peptide 19	[H]KCEQFVGPLTVNEKR[OH]
	Peptide 20	[H]VGPLTVNEKRRLQLI[OH]
Polymerase pool 2	Peptide 21	[H]VNEKRRLQLIMPARF[OH]
	Peptide 22	[H]RLQLIMPARFYPKVT[OH]
	Peptide 23	[H]MPARFYPKVTKYLPL[OH]
	Peptide 24	[H]YPKVTKYLPLDKGIK[OH]
	Peptide 25	[H]KYLPLDKGIKPYYPE[OH]
	Peptide 26	[H]DKGIKPYYPEHLVNH[OH]
	Peptide 27	[H]PYYPEHLVNHYFQTR[OH]
	Peptide 28	[H]HLVNHYFQTRHYLHT[OH]
	Peptide 29	[H]YFQTRHYLHTLWKAG[OH]
	Peptide 30	[H]HYLHTLWKAGILYKR[OH]
	Peptide 31	[H]LWKAGILYKRETTHS[OH]

	Peptide 32	[H]ILYKRETTHSASFCG[OH]
	Peptide 33	[H]ETTHSASFCGSPYSW[OH]
	Peptide 34	[H]ASFCGSPYSWEQDLQ[OH]
	Peptide 35	[H]SPYSWEQDLQHGAES[OH]
	Peptide 36	[H]EQDLQHGAESFHQQS[OH]
	Peptide 37	[H]HGAESFHQQSSGILS[OH]
	Peptide 38	[H]FHQQSSGILSRPPVG[OH]
	Peptide 39	[H]SGILSRPPVGSSLQS[OH]
	Peptide 40	[H]RPPVGSSLQSKHSKS[OH]
Polymerase pool 3	Peptide 41	[H]SSLQSKHSKSRLGLQ[OH]
	Peptide 42	[H]KHSKSRLGLQSQQGH[OH]
	Peptide 43	[H]RLGLQSQQGHLARRQ[OH]
	Peptide 44	[H]SQQGHLARRQQGRSW[OH]
	Peptide 45	[H]LARRQQGRSWSIRAG[OH]
	Peptide 46	[H]QGRSWSIRAGFHPTA[OH]
	Peptide 47	[H]SIRAGFHPTARRPFG[OH]
	Peptide 48	[H]FHPTARRPFGVEPSG[OH]
	Peptide 49	[H]RRPFGVEPSGSGHTT[OH]
	Peptide 50	[H]VEPSGSGHTTNFASK[OH]
	Peptide 51	[H]SGHTTNFASKSASCL[OH]
	Peptide 52	[H]NFASKSASCLHQSPD[OH]
	Peptide 53	[H]SASCLHQSPDRKAAY[OH]
	Peptide 54	[H]HQSPDRKAAYPAVST[OH]
	Peptide 55	[H]RKAAYPAVSTFEKHS[OH]
	Peptide 56	[H]PAVSTFEKHSSSGHA[OH]
	Peptide 57	[H]FEKHSSSGHAVEFHN[OH]
	Peptide 58	[H]SSGHAVEFHNLSPNS[OH]
	Peptide 59	[H]VEFHNLSPNSARSQS[OH]
	Peptide 60	[H]LSPNSARSQSERPVF[OH]
Polymerase pool 4	Peptide 61	[H]ARSQSERPVFPCWWL[OH]
	Peptide 62	[H]ERPVFPCWWLQFRSS[OH]
	Peptide 63	[H]PCWWLQFRSSKPCSD[OH]
	Peptide 64	[H]QFRSSKPCSDYCLSL[OH]
	Peptide 65	[H]KPCSDYCLSLIVNLL[OH]
	Peptide 66	[H]YCLSLIVNLLEDWGP[OH]
	Peptide 67	[H]IVNLLEDWGPCAEHG[OH]
	Peptide 68	[H]EDWGPCAEHGEHHIR[OH]
	Peptide 69	[H]CAEHGEHHIRIPRTP[OH]
	Peptide 70	[H]EHHIRIPRTPSRVTG[OH]
	Peptide 71	[H]IPRTPSRVTGGVFLV[OH]
	Peptide 72	[H]SRVTGGVFLVDKNPH[OH]
	Peptide 73	[H]GVFLVDKNPHNTAES[OH]
	Peptide 74	[H]DKNPHNTAESRLVVD[OH]

	Peptide 75	[H]NTAESRLVVDFSQFS[OH]
	Peptide 76	[H]RLVVDFSQFSRGNYR[OH]
	Peptide 77	[H]FSQFSRGNYRVSWPK[OH]
	Peptide 78	[H]RGNYRVSWPKFAVPN[OH]
	Peptide 79	[H]VSWPKFAVPNLQSLT[OH]
	Peptide 80	[H]FAVPNLQSLTNLLSS[OH]
	Peptide 81	[H]LQSLTNLLSSNLSWL[OH]
Polymerase pool 5	Peptide 82	[H]NLLSSNLSWLSLDVS[OH]
	Peptide 83	[H]NLSWLSLDVSAAFYH[OH]
	Peptide 84	[H]SLDVSAAFYHLPLHP[OH]
	Peptide 85	[H]AAFYHLPLHPAAMPH[OH]
	Peptide 86	[H]LPLHPAAMPHLLVGS[OH]
	Peptide 87	[H]AAMPHLLVGSSGLSR[OH]
	Peptide 88	[H]LLVGSSGLSRYVARL[OH]
	Peptide 89	[H]SGLSRYVARLSSNSR[OH]
	Peptide 90	[H]YVARLSSNSRILNHQ[OH]
	Peptide 91	[H]SSNSRILNHQHGTMP[OH]
	Peptide 92	[H]ILNHQHGTMPNLHDY[OH]
	Peptide 93	[H]HGTMPNLHDYCSRNL[OH]
	Peptide 94	[H]NLHDYCSRNLYVSLL[OH]
	Peptide 95	[H]CSRNLYVSLLLLYQT[OH]
	Peptide 96	[H]YVSLLLLYQTFGRKL[OH]
	Peptide 97	[H]LLYQTFGRKLHLYSH[OH]
	Peptide 98	[H]FGRKLHLYSHPIILG[OH]
	Peptide 99	[H]HLYSHPIILGFRKIP[OH]
	Peptide 100	[H]PIILGFRKIPMGVGL[OH]
	Peptide 101	[H]FRKIPMGVGLSPFLL[OH]
	Peptide 102	[H]MGVGLSPFLLAQFTS[OH]
Polymerase pool 6	Peptide 103	[H]SPFLLAQFTSAICSV[OH]
	Peptide 104	[H]AQFTSAICSVVRRAF[OH]
	Peptide 105	[H]AICSVVRRAFPHCLA[OH]
	Peptide 106	[H]VRRAFPHCLAFSYMD[OH]
	Peptide 107	[H]PHCLAFSYMDDVVLG[OH]
	Peptide 108	[H]FSYMDDVVLGAKSVQ[OH]
	Peptide 109	[H]DVVLGAKSVQHLESL[OH]
	Peptide 110	[H]AKSVQHLESLFTAVT[OH]
	Peptide 111	[H]HLESLFTAVTNFLLS[OH]
	Peptide 112	[H]FTAVTNFLLSLGIHL[OH]
	Peptide 113	[H]NFLLSLGIHLNPNKT[OH]
	Peptide 114	[H]LGIHLNPNKTKRWGY[OH]
	Peptide 115	[H]NPNKTKRWGYSLNFM[OH]
	Peptide 116	[H]KRWGYSLNFMGYVIG[OH]
	Peptide 117	[H]SLNFMGYVIGSYGSL[OH]

	Peptide 118	[H]GYVIGSYGSLPQEHI[OH]
	Peptide 119	[H]SYGSLPQEHIIQKIK[OH]
	Peptide 120	[H]PQEHIIQKIKECFRK[OH]
	Peptide 121	[H]IQKIKECFRKLPINR[OH]
	Peptide 122	[H]ECFRKLPINRPIDWK[OH]
	Peptide 123	[H]LPINRPIDWKVCQRI[OH]
Polymerase pool 7	Peptide 124	[H]PIDWKVCQRIVGLLG[OH]
	Peptide 125	[H]VCQRIVGLLGFAAPF[OH]
	Peptide 126	[H]VGLLGFAAPFTQCGY[OH]
	Peptide 127	[H]FAAPFTQCGYPALMP[OH]
	Peptide 128	[H]TQCGYPALMPLYACI[OH]
	Peptide 129	[H]PALMPLYACIQSKQA[OH]
	Peptide 130	[H]LYACIQSKQAFTFSP[OH]
	Peptide 131	[H]QSKQAFTFSPTYKAF[OH]
	Peptide 132	[H]FTFSPTYKAFLCKQY[OH]
	Peptide 133	[H]TYKAFLCKQYLNLYP[OH]
	Peptide 134	[H]LCKQYLNLYPVARQR[OH]
	Peptide 135	[H]LNLYPVARQRPGLCQ[OH]
	Peptide 136	[H]VARQRPGLCQVFADA[OH]
	Peptide 137	[H]PGLCQVFADATPTGW[OH]
	Peptide 138	[H]VFADATPTGWGLVMG[OH]
	Peptide 139	[H]TPTGWGLVMGHQRVR[OH]
	Peptide 140	[H]GLVMGHQRVRGTFSA[OH]
	Peptide 141	[H]HQRVRGTFSAPLPIH[OH]
	Peptide 142	[H]GTFSAPLPIHTAELL[OH]
	Peptide 143	[H]PLPIHTAELLAACFA[OH]
	Peptide 144	[H]TAELLAACFARSRSG[OH]
Polymerase pool 8	Peptide 145	[H]AACFARSRSGANIIG[OH]
	Peptide 146	[H]RSRSGANIIGTDNSV[OH]
	Peptide 147	[H]ANIIGTDNSVVLSRK[OH]
	Peptide 148	[H]TDNSVVLSRKYTSYP[OH]
	Peptide 149	[H]VLSRKYTSYPWLLGC[OH]
	Peptide 150	[H]YTSYPWLLGCAANWI[OH]
	Peptide 151	[H]WLLGCAANWILRGTS[OH]
	Peptide 152	[H]AANWILRGTSFVYVP[OH]
	Peptide 153	[H]LRGTSFVYVPSALNP[OH]
	Peptide 154	[H]FVYVPSALNPADDPS[OH]
	Peptide 155	[H]SALNPADDPSRGRLG[OH]
	Peptide 156	[H]ADDPSRGRLGLSRPL[OH]
	Peptide 157	[H]RGRLGLSRPLLRLPF[OH]
	Peptide 158	[H]LSRPLLRLPFRPTTG[OH]
	Peptide 159	[H]LRLPFRPTTGRTSLY[OH]
	Peptide 160	[H]RPTTGRTSLYADSPS[OH]

	Peptide 161	[H]RTSLYADSPSVPSHL[OH]
	Peptide 162	[H]ADSPSVPSHLPDRVH[OH]
	Peptide 163	[H]VPSHLPDRVHFASPL[OH]
	Peptide 164	[H]PDRVHFASPLHVAWR[OH]
	Peptide 165	[H]RVHFASPLHVAWRPP[OH]

Supplementary Table 2. Study cohort of HBeAg negative patients with chronic HBV infection divided based on therapy status.

Characteristics	Patients with chronic HBV infection (n=57)	
	With therapy	Without therapy
Number of patients	18	39
HBsAg (IU/mL): median (range)	1,195.5 (18-45634)	1,710 (0.2-31,677)
HBcrAg (Log U/ml): median (range)	3.0 (2.0-8.2)	2.6 (2-7.3)
Sex (male/female)	12/6	22/17
Age (years): median (range)	43 (22-60)	42 (18-72)
ALT level (IU/L): median (range)	26 (15-58)	26 (13-194)
HBV DNA <2,000 IU/mL (%)	83.3	76.9
HBeAg (-/+/n.d.)	16/0/2	38/0/1
NA therapy yes/ no	18/0	0/39

Supplementary Table 3. Study cohort of HBeAg negative patients with chronic HBV infection divided based on HBV DNA titer and ALT level.

Characteristics	Patients with chronic HBV infection (n=57)			
	HBV DNA <2000 IU/mL & ALT level normal	HBV DNA >2000 IU/mL & ALT level normal	HBV DNA <2000 IU/mL & ALT level upper limit of normal	HBV DNA >2000 IU/mL & ALT level upper limit of normal
Number of patients	36	7	9	5
HBsAg (IU/mL): median (range)	595 (0.2-31,677)	11,830 (39-45,634)	1,301 (1-34,727)	6996 (1,590-20,941)
HBcrAg (Log U/ml): median (range)	2.6 (2-5.5)	3.1 (2-8.2)	2.8 (2-5.1)	5.7 (4.2-7.3)
Sex (male/female)	21/15	3/4	6/3	4/1
Age (years): median (range)	42.5 (18-72)	33 (18-46)	35 (19-60)	49 (33-67)
ALT level (IU/L): median (range)	23.5 (13-44)	24 (19-40)	54 (42-112)	128 (66-220)
NA therapy yes/ no	12/24	2/5	3/6	1/4

SUPPLEMENTARY FIGURE LEGENDS

Supplementary figure S1. Overview of the study design.

Schematic representation of the study design for (A) phenotyping of total immune cells and functional study of HBV-specific T cell and (B) phenotyping and functional study of HBV $core_{18}$- and HBV pol_{455}-specific T cells of HLA-A*02 positive, chronic hepatitis B infected patients. HBcrAg, hepatitis B core-related antigen; HBsAg, hepatitis B virus surface antigen; rhIL-2, recombinant human interleukin-2; pMHC I, peptide-loaded MHC I.

Supplementary figure S2. Characterization of total T cells in CHB patients with different levels of HBsAg and HBcrAg.

(A) Gating strategies used to identify *ex vivo* $CD4^+$ and $CD8^+$ T cells and downstream analysis of activation and exhaustion phenotypes and T cell subsets based on CD45RA and CCR7 expression; naïve ($CD45RA^+$ $CCR7^+$), T_{CM}: central memory ($CD45RA^-$ $CCR7^+$), T_{EM}: effector memory ($CD45RA^-$ $CCR7^-$), T_{EMRA}: terminally differentiated effector memory (T_{EMRA}; $CD45RA^+$ $CCR7^-$). (B-C) Correlation of HBsAg level (B) and HBcrAg level (C) with $CD4^+$ and $CD8^+$ T cell subsets. (D) Frequencies of γδ T cells, MAIT cells and Treg cells in CHB patients with different levels of HBsAg or HBcrAg. Radar plot depicting the mean percentage of total T cell subsets from each group of patients with different levels of HBsAg or HBcrAg. Statistical significance between each two groups was tested by Mann-Whitney test for non-parametric data and by Unpaired t test for parametric data.

Supplementary figure S3. Correlation analysis of HBsAg and HBcrAg with HBV-specific CD4$^+$ and CD8$^+$ T cell response.

HBV-specific CD4$^+$ and CD8$^+$ T cell responses following 10-day *in vitro* stimulation with HBV OLP pools. (A-B) Correlation of HBsAg (A) and HBcrAg (B) with total, core-, surface-, and polymerase-specific T cell response. Total-specific T cell response: sum of all 14 OLP pools.

Supplementary figure S4. Influence of NA therapy, HBV DNA titer and ALT level on HBV-specific CD4$^+$ and CD8$^+$ T cell responses in CHB patients.

HBV-specific CD4$^+$ and CD8$^+$ T cell responses following 10-day *in vitro* stimulation with HBV OLP pools. (A) Expression of IFN-γ by HBV-specific CD4$^+$ and CD8$^+$ T cells from NA treated (n=18) and untreated (n=39) CHB patients. (B) Comparison of IFN-γ expressing HBV-specific T cells in different stages of disease grouped according to HBV DNA titer and ALT levels. Statistical significance was tested by Mann-Whitney test for non-parametric data and by Unpaired t test for parametric data.

Supplementary figure S5. Correlation analyses of age with HBsAg and HBcrAg as well as CD4$^+$ and CD8$^+$ T cell subsets.

(A) Correlation analyses of the age and quantities of HBsAg and HBcrAg. (B) Correlation analyses of the age and frequencies of CD4$^+$ and CD8$^+$ T cell subsets.