

Electronic Supplementary Material

New Gene Variants Associated With the Risk of Chronic HBV Infection

Mengjie Fan^{1#}, Jing Wang^{2,3#}, Sa Wang^{1#}, Tengyan Li³, Hong Pan³, Hankui Liu^{4,5}, Huifang Xu^{4,5}, Daria V. Zhernakova⁶, Stephen J. O'Brien^{6,7}, Zhenru Feng⁸, Le Chang⁸, Erhei Dai⁹, Jianhua Lu⁹, Hongli Xi¹, Yanyan Yu¹, Jianguo Zhang^{4,5}✉, Binbin Wang³✉, Zheng Zeng¹✉

1. Department of Infectious Diseases, Peking University First Hospital, Beijing, 100034, China
2. Department of Medical Genetics and Development Biology, School of Medical Basic, Capital Medical University, Beijing, 100069, China
3. Center for Genetics, National Research Institute for Family Planning, Beijing, 100081, China
4. BGI-Shenzhen, Shenzhen 518083, China
5. BGI Genomics, BGI-Shenzhen, Shenzhen 518083, China
6. Laboratory of Genomic Diversity, Center for Computer Technologies, ITMO University, St. Petersburg, 197101, Russia
7. Guy Harvey Oceanographic Center, Halmos College of Natural Sciences and Oceanography, Nova Southeastern University, Ft Lauderdale, Florida 33004, USA
8. Department of Laboratory Medicine, Peking University First Hospital, Beijing, 100034, China
9. The Fifth Hospital of Shijiazhuang, Shijiazhuang 050024, China

#These authors contributed equally to the manuscript.

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Supplementary Table S1 The first 150 potentially functional variations ranked by *P* value of whole exome sequencing

Position	Variant type	Gene	SNP	Case MAF	Control MAF	Change	<i>P</i> value
chr4:88583405	missense	DMP1	rs79402270	0.01485	0.1139	C>A	5.29E-05
chrX:47062534	missense	UBA1	rs2070169	0.07921	0.2059	G>A	3.31E-04
chr2:179474668	missense	TTN	rs16866412	0.0495	0.1569	G>A	4.92E-04
chr4:128842876	missense	MFSB8	rs11098943	0.04455	0.1471	C>G	5.94E-04
chr3:169569432	missense	LRR31	rs35923425	0.09901	0.01961	C>G	6.15E-04
chrX:27839572	missense	MAGEB10	rs1368769	0.0198	0.1029	T>C	6.35E-04
chr11:113194168	missense	TTC12	rs723077	0.3416	0.5098	A>C	6.54E-04
chr15:74622533	missense	CCDC33	rs2277603	0.1684	0.3168	A>G	6.73E-04
chr9:114359624	missense	PTGR1	rs1053959	0.2525	0.4118	A>C	7.41E-04
chr11:61669946	missense	RAB3IL1	rs3815045	0.28	0.1422	G>A	9.13E-04
chr3:179322385	missense	MRPL47	rs2339844	0.08416	0.201	A>C	9.85E-04
chr1:19609254	missense	AKR7A3	rs1738025	0.285	0.1471	C>T	1.012E-03
chr19:1796166	missense	ATP8B3	rs8100856	0.5396	0.3775	T>C	1.405E-03
chr19:39760435	missense	IFNL2	rs59746524	0.03646	0.125	T>C	1.462E-03
chr19:52393984	missense	ZNF649	rs1433083	0.1089	0.02941	C>T	1.559E-03
chr2:179515483	missense	TTN	rs72650066	0.04455	0.1386	G>C	1.581E-03
chr10:23393091	missense	MSRB2	rs2296466	0.09901	0.2157	A>G	1.597E-03
chr13:92345579	missense	GPC5	rs553717	0.3416	0.198	C>T	1.629E-03
chr19:52376507	missense	ZNF577	rs2288868	0.3416	0.201	T>C	1.723E-03
chr5:149008467	missense	ARHGEF37	rs3733662	0.38	0.2353	C>A	1.766E-03
chr6:117710661	missense	ROS1	rs28639589	0.1238	0.03922	T>C	1.872E-03
chr5:79616083	missense	SPZ1	rs1862136	0.08911	0.01961	C>G	1.917E-03
chrX:13681115	missense	TCEANC	rs2361159	0.4406	0.2892	T>C	1.939E-03
chr9:35674053	missense	CA9	rs2071676	0.41	0.5637	A>G	2.088E-03
chr10:33475282	missense	NRP1	rs2228638	0.1584	0.05941	C>T	2.108E-03
chr17:48456193	missense	EME1	rs12450550	0.04455	0.1324	T>C	2.569E-03
chr1:204589101	missense	LRRN2	rs3789044	0.2376	0.3775	G>A	2.592E-03
chr2:48010488	missense	MSH6	rs1042821	0.1634	0.2921	G>A	2.891E-03
chr6:153323594	missense	MTRF1L	rs3818123	0.396	0.5441	T>C	2.93E-03
chr11:122646967	missense	UBASH3B	rs12790613	0.27	0.145	G>A	2.936E-03
chr3:155571275	missense	SLC33A1	rs3804769	0.2178	0.1078	T>C	3.001E-03
chr8:117950768	missense	AARD	rs16889283	0.155	0.2806	G>C	3.298E-03
chr3:9506285	missense	SETD5	rs117354149	0.08416	0.01961	T>C	3.331E-03
chr11:6585007	missense	DNHD1	rs11040923	0.3663	0.2304	A>G	3.336E-03
chr5:150565008	missense	CCDC69	.	0.2772	0.4208	C>T	3.401E-03
chr19:10088271	missense	COL5A3	rs2161468	0.4901	0.3431	C>G	3.451E-03
chr11:94861862	missense	ENDOD1	rs75384502	0.1089	0.03431	A>G	3.671E-03
chr3:194062519	missense	CPN2	rs3732477	0.38	0.2451	C>T	3.761E-03
chr1:17914122	missense	ARHGEF10L	rs35497285	0.1188	0.2304	G>A	3.868E-03
chr21:46057548	missense	KRTAP10-10	rs4818947	0.2475	0.3824	C>A	3.918E-03
chr11:60165352	frameshift	MS4A14	rs3217518	0.45	0.3088	A>ATT	4.056E-03
chr21:46077946	missense	KRTAP12-3	rs9306111	0.2525	0.3873	G>A	4.074E-03
chr19:2226772	missense	DOT1L	rs2302061	0.3911	0.2549	G>C	4.091E-03
chr5:32090294	missense	PDZD2	rs10066063	0.3168	0.1912	G>A	4.283E-03
chr14:20470852	frameshift	OR4Q2	rs34315947	0.1683	0.2892	C>CT	4.491E-03
chr21:46057806	missense	KRTAP10-10	rs4818950	0.2673	0.402	A>G	4.536E-03
chr16:56500132	missense	OGFOD1	rs34883368	0.09406	0.1961	C>T	4.58E-03
chr19:10446568	missense	ICAM3	rs2304237	0.1139	0.2206	T>C	5.03E-03
chr19:10449358	missense	ICAM3	rs7258015	0.1139	0.2206	T>C	5.03E-03
chr21:46066764	missense	KRTAP10-11	rs4818952	0.29	0.4265	T>C	5.062E-03
chrX:118587003	missense	SLC25A43	rs3810755	0.3663	0.5049	T>C	5.175E-03
chr10:64927823	missense	JMJD1C	rs1935	0.21	0.3382	C>G	5.201E-03
chr1:203768328	missense	ZBED6	rs7552670	0.2475	0.3775	T>C	5.38E-03
chr6:154360797	missense	OPRM1	rs1799971	0.2475	0.3775	A>G	5.38E-03

chr6:12124587	missense	HIVEP1	rs2228212	0.1634	0.07353	C>G	5.557E-03
chrX:75649340	missense	MAGEE1	rs7051260	0.0198	0.08333	G>C	5.849E-03
chr12:117383320	missense	FBXW8	rs4076700	0.2228	0.348	A>G	5.992E-03
chr7:143043240	missense	CLCN1	rs13438232	0.2574	0.1465	C>T	6.225E-03
chr17:48432324	missense	XYLT2	rs12451299	0.04455	0.1225	G>C	6.465E-03
chr10:64974537	missense	JMJD1C	rs10761725	0.235	0.3627	A>T	6.501E-03
chr14:106878056	missense	IGHV4-39	rs4774113	0.134	0.2424	T>G	6.708E-03
chr2:186668935	missense	FSIP2	rs13003744	0.4158	0.2843	A>G	6.741E-03
chr10:85981842	missense	LRIT2	rs12217769	0.3713	0.2426	A>G	6.877E-03
chr3:123419573	missense	MYLK	rs3732487	0.5297	0.3911	T>G	6.962E-03
chr19:50412217	missense	NUP62	rs1062798	0.5198	0.3824	C>G	7.005E-03
chr1:204587569	missense	LRRN2	rs3747631	0.245	0.3725	G>C	7.019E-03
chrX:19375782	missense	PDHA1	rs2229137	0.2376	0.1324	A>C	7.159E-03
chr6:12123249	missense	HIVEP1	rs2228220	0.1139	0.2157	A>G	7.227E-03
chr13:44411432	missense	CCDC122	rs9567280	0.06931	0.1569	A>G	7.265E-03
chrX:69478421	missense	P2RY4	rs72628860	0.0297	0.09804	G>T	7.304E-03
chrX:69478736	missense	P2RY4	rs56217451	0.0297	0.09804	T>C	7.304E-03
chr1:204587047	missense	LRRN2	rs11588857	0.2475	0.3725	G>A	7.324E-03
chr6:167592524	missense	TCPI0L2	rs2989545	0.42	0.5539	C>T	7.383E-03
chr16:89849480	missense	FANCA	rs2239359	0.2673	0.1569	T>C	7.457E-03
chr10:19676553	missense	MALRD1	rs12773592	0.08416	0.1765	A>G	7.596E-03
chr10:19676561	missense	MALRD1	rs12771333	0.08416	0.1765	G>A	7.596E-03
chr1:46500728	missense	MAST2	rs3737738	0.1386	0.05882	G>A	7.622E-03
chr11:114568942	missense	NXPE2	rs11215158	0.1436	0.05941	T>C	7.738E-03
chr13:25009485	missense	PARP4	rs1050110	0.225	0.35	C>G	7.867E-03
chr2:135988235	missense	ZRANB3	rs76333606	0.1238	0.04902	C>T	7.906E-03
chr2:163137983	missense	IFIH1	rs10930046	0.1238	0.04902	T>C	7.906E-03
chr10:85981801	missense	LRIT2	rs6585847	0.455	0.3235	T>G	7.928E-03
chr17:65052304	missense	CACNG1	rs1799938	0.1139	0.04	G>A	7.952E-03
chr2:179589058	missense	TTN	rs72648960	0.0495	0.1275	G>A	8.074E-03
chr7:107002806	missense	COG5	rs2269970	0.2624	0.3873	G>A	8.105E-03
chr13:25009297	missense	PARP4	rs1050112	0.2277	0.3515	G>T	8.326E-03
chr4:74451073	missense	RASSF6	rs12507775	0.07426	0.1618	A>G	8.467E-03
chr12:49434409	missense	KMT2D	rs3741626	0.02475	0.08824	G>A	8.609E-03
chr3:167000256	missense	ZBBX	rs12638625	0.2723	0.3971	C>G	8.612E-03
chr8:145641328	missense	SLC39A4	rs17855765	0.4901	0.3578	C>T	8.936E-03
chr1:11856378	missense	MTHFR	rs1801133	0.3515	0.4804	A>G	8.999E-03
chr14:107013129	missense	IGHV3-49	rs2073674	0.51	0.3775	A>C	9.141E-03
chr4:38774889	missense	TLR10	rs4129009	0.505	0.3725	T>C	9.224E-03
chr19:58880242	missense	ZNF837	rs7256940	0.3614	0.2402	T>C	9.296E-03
chr1:94496053	missense	ABCA4	rs1800549	0.09901	0.03431	G>A	9.574E-03
chr3:194061826	missense	CPN2	rs11711157	0.3663	0.2451	C>T	9.626E-03
chr22:19183787	missense	CLTCL1	rs1633399	0.1139	0.04412	A>G	9.883E-03
chr22:19195680	missense	CLTCL1	rs807547	0.1139	0.04412	T>C	9.883E-03
chr22:19197949	missense	CLTCL1	rs712952	0.1139	0.04412	G>A	9.883E-03
chr1:36888462	missense	OSCP1	rs1416840	0.2129	0.3317	A>G	9.971E-03
chr19:52620269	missense	ZNF616	rs35582075	0.1188	0.04455	G>A	1.003E-02
chr9:133963008	missense	LAMC3	rs4740412	0.04455	0.1176	G>A	1.008E-02
chr7:138764060	missense	ZC3HAV1	rs2236424	0.4257	0.5539	A>G	1.011E-02
chr7:95034775	missense	PON2	rs7493	0.1139	0.2108	G>C	1.028E-02
chr7:95041016	missense	PON2	rs12026	0.1139	0.2108	G>C	1.028E-02
chrX:130412018	missense	IGSF1	rs146715796	0.1139	0.2108	C>G	1.028E-02
chr15:33381000	missense	FMN1	rs2291065	0.2165	0.1188	A>T	1.034E-02
chr9:129958862	missense	RALGPS1	rs57728614	0.1485	0.06863	G>T	1.059E-02
chr22:50555686	missense	MOV10L1	rs760749	0.2673	0.1618	A>C	1.101E-02
chr3:97983265	missense	OR5H6	rs4241472	0.4105	0.5408	C>A	1.104E-02
chr19:14083761	missense	RFX1	rs2305780	0.4604	0.3333	T>C	1.111E-02
chr6:66204945	missense	EYS	rs12193967	0.34	0.2255	G>A	1.12E-02
chr6:12125772	missense	HIVEP1	rs1126472	0.1188	0.2157	A>G	1.125E-02
chr14:100375707	missense	EML1	rs34198557	0.4	0.2772	C>T	1.132E-02

chr19:58879660	missense	ZNF837	rs61746138	0.3557	0.2376	T>C	1.132E-02
chr6:146243916	missense	SHPRH	rs118070529	0.1337	0.05882	T>C	1.151E-02
chr11:94261280	missense	LOC643037	rs11605546	0.08911	0.02941	G>A	1.161E-02
chr14:64557725	missense	SYNE2	rs76576553	0.08911	0.02941	C>G	1.161E-02
chr12:53186088	missense	KRT3	rs3887954	0.1535	0.07353	G>C	1.222E-02
chr2:228883721	missense	SPHKAP	rs3811514	0.29	0.4118	C>T	1.233E-02
chr19:10084292	missense	COL5A3	rs2287813	0.505	0.3775	C>G	1.236E-02
chr8:21550858	missense	GFRA2	rs77601365	0.0495	0.1225	G>A	1.238E-02
chr7:35709842	missense	HERPUD2	rs3779234	0.25	0.1485	C>T	1.241E-02
chr3:124731689	missense	HEG1	rs78680419	0.5248	0.3971	T>A	1.271E-02
chr5:32087374	missense	PDZD2	rs157496	0.3812	0.5049	A>G	1.275E-02
chr3:124732618	missense	HEG1	rs6790837	0.396	0.5196	A>G	1.304E-02
chr1:203769532	missense	ZBED6	rs7540041	0.2475	0.3627	G>A	1.323E-02
chr6:43184132	missense	CUL9	rs2273709	0.302	0.4216	A>C	1.332E-02
chr4:2951804	missense	NOP14	rs2515960	0.2525	0.152	A>G	1.336E-02
chr2:186603605	frameshift	FSIP2	rs35617283	0.4307	0.3088	A>AG	1.35E-02
chr5:170239112	missense	GABRP	rs1063310	0.215	0.3267	C>A	1.354E-02
chr12:51442944	missense	LETMD1	rs12379	0.06436	0.1422	A>G	1.377E-02
chr14:58605790	missense	C14orf37	rs3829765	0.3119	0.4314	G>A	1.387E-02
chr9:271638	missense	DOCK8	rs506121	0.4406	0.3186	C>T	1.4E-02
chr7:154989982	missense	AC099552.4	rs28664023	0.22	0.3333	G>A	1.428E-02
chr16:23080634	missense	USP31	rs10083789	0.095	0.03431	C>A	1.472E-02
chr22:50684415	missense	HDAC10	rs11553697	0.1386	0.2353	T>C	1.537E-02
chr17:74878259	missense	MGAT5B	rs571264	0.4091	0.29	G>A	1.55E-02
chr4:88583135	missense	DMP1	rs10019009	0.495	0.3713	A>T	1.559E-02
chr9:37503087	missense	POLR1E	rs10814571	0.197	0.302	G>A	1.574E-02
chr5:73218954	missense	ARHGEF28	rs423333	0.06931	0.1471	C>T	1.59E-02
chr12:21713402	missense	GYS2	rs2306180	0.2327	0.3431	C>T	1.593E-02
chr5:145442133	missense	SH3RF2	rs11435	0.2376	0.3515	G>A	1.615E-02
chr2:152536498	missense	NEB	rs6735208	0.54	0.4158	T>A	1.645E-02
chr18:33557466	missense	C18orf21	rs2276314	0.3515	0.2402	A>G	1.664E-02
chr5:149001551	missense	ARHGEF37	rs4629585	0.5198	0.3971	C>A	1.671E-02
chr19:55281315	missense	KIR2DL1	rs2304224	0.13	0.05882	G>T	1.672E-02
chr4:187120211	missense	CYP4V2	rs13146272	0.3	0.4158	C>A	1.689E-02
chr19:10224548	missense	PPAN- P2RY11	rs3745601	0.3	0.4158	G>A	1.689E-02
chr17:37814080	missense	STARD3	rs1877031	0.5396	0.4167	G>A	1.699E-02

Note: SNP, single nucleotide polymorphism.

Supplementary table S2 Characteristics of those published CHB risk-associated SNPs (Chang *et al.* 2014)

Variant and risk allele	Mapped gene	Reported trait	Location	Performance in our first stage population (<i>P</i> -value) (*)
rs7453920-G, rs9277535-G, rs7756516-T, rs9276370-T, rs9366816-T	HLA-DQB2; HLA-DPB1; HLA-DQB2; HLA-DQB3- HLA-DQA2; HLA-DPA3	Chronic hepatitis B infection	Intron; 3' UTR; 3' UTR; 5' near gene; Intron	- - - - -
rs9276370-T	HLA-DQB3, HLA-DQA2	Chronic hepatitis B infection	5' near gene	-
rs7453920-G	HLA-DQB2	Chronic hepatitis B infection	Intron	-
rs9277535-G	HLA-DPB1	Chronic hepatitis B infection	3' UTR	-
rs9366816-C	HLA-DPA3	Chronic hepatitis B infection	Intron	-

Note: *, We conducted a whole-exome sequencing analysis in our first stage, so the performance of those loci that are not in the exome capture region are unavailable.

Chang SW, Fann CS, Su WH, Wang YC, Weng CC, Yu CJ, Hsu CL, Hsieh AR, Chien RN, Chu CM, Tai DI (2014) A genome-wide association study on chronic HBV infection and its clinical progression in male Han-Taiwanese. PLoS One 9: e99724