Supporting Information for

Role of Humoral Immunity against Hepatitis B Virus Core Antigen in the Pathogenesis of Acute Liver Failure

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SI Materials and Methods

Patients. At the time of liver transplantation, for each of the 4 patients with ALF we obtained serum and 4 liver specimens for Patient 241, 4 for Patient 31, 5 for Patient 219 and 4 for Patient 32. Serum and individual specimens were also obtained from each of the 17 controls. Liver and serum specimens, along with the clinical data, were received under code to protect the identity of the subjects. The diagnosis of HBV-associated ALF was based on the presence of serum hepatitis B surface antigen (HBsAg) and/or IgM antibody to hepatitis B core (anti-HBc IgM). At admission, all patients with ALF were tested for antibodies against hepatitis A, B, C and D, cytomegalovirus, Epstein Barr virus and human immunodeficiency virus (HIV), as well as hepatitis C virus (HCV) and hepatitis D virus (HDV) RNA, and all were negative. Each liver specimen, obtained from patients with ALF or controls, was divided into two pieces: one was snap frozen and the other was formalin-fixed and paraffin-embedded (FFPE). Snap-frozen samples were stored at -80°C for molecular studies, including mRNA and microRNA-expression profiling, next-generation sequencing, and phage display library. Fixed liver tissue was used for immunohistochemistry and pathological examination by two expert hepatopathologists (D.E.K. and S.G.).

Serology. All patients were tested for standard HBV serology as well as for titers of HBsAg, IgM and IgG anti-HBc. Serum HBsAg, anti-HBs, antibody to hepatitis B core antigen (anti-HBc), IgM anti-HBc, hepatitis B e antigen (HBeAg), anti-HBe, IgM antibody to HAV, Epstein-Barr virus, and cytomegalovirus, anti-HCV, and anti-HIV were measured with commercial enzyme immunoassays (Abbott Laboratories). Titers of IgM and IgG anti-HBc were determined with enzyme immunoassays by testing 2-fold serial dilutions. HBsAg was quantified by reference to the US Bureau of Biologics internal standard. IgG and IgM anti-HDV were measured with commercial enzyme immunoassays (Sorin Biomedica). Serum HBV DNA was quantified by a commercial assay (Amplicor HBV Monitor test; Roche

Diagnostics). Serum HDV RNA was determined by PCR (1) and serum HCV RNA by a commercial assay (Cobas Amplicor HCV Monitor 2.0; Roche Diagnostics).

Chimpanzees. Due to ethical reasons, the study of liver specimens during the acute phase of viral hepatitis in humans is not possible. Acute hepatitis B in chimpanzees has been studied extensively in chimpanzees and it was demonstrated to be virtually identical to that seen in humans (2, 3). To compare ALF with classic acute hepatitis B, we studied two chimpanzees previously infected with HBV (ayw) (2, 3). The virologic course of acute HBV infection, the T-cell immune responses, and the gene expression profiling were reported previously (2, 3). Here, we assessed the levels of serum HBV DNA, HBeAg and the titer of IgG and IgM anti-HBc throughout the disease course, the liver pathology in serial archival liver biopsies throughout the course of HBV infection, analyzed the intrahepatic expression of specific cell lineage markers at three time points during the acute infection (Ch. 5835: week 6, 18, and 20; Ch.1627: week 10, 14, and 20), and generated phage-display Fab libraries using RNA extracted from stored liver specimens of each animal at the time of viral clearance (Ch. 5835: week 18; Ch.1627: week 14, and 16). The phage display libraries were panned against the autologous HBsAg and HBcAg. The Fab fragments were sequenced and their affinity was studied by using surface plasmon resonance (SPR) on a Biacore 3000 (GE Healthcare, Piscataway, NJ).

Serum and liver DNA extraction and real-time polymerase chain reaction. Total DNA was purified from serum samples using QIAamp DNA Blood Mini Kit (Qiagen, Hilden, Germany), and from liver specimens using Qiagen DNeasy kit (Qiagen). The levels of HBV DNA were determined in serum and liver using a real-time PCR, as previously reported (4). Liver total RNA was extracted from stored frozen liver specimens using TRIzol reagent (Invitrogen, Carlsbad, CA) according to the manufacturer's recommendations. The

intrahepatic amounts of HBV DNA and HBV RNA, were determined using PCR assays as previously reported (5, 6) with minor modifications.

Full genome hepatitis B virus next-generation sequencing. To investigate the genetic heterogeneity of HBV strains associated with ALF, HBV full-genome sequencing was performed both in serum and liver of each of the 4 patients with this disease using next-generation sequencing. Viral DNA was purified from serum using the QIAamp DNA Blood Mini Kit (Qiagen, Valencia, CA) and liver specimens using Qiagen DNeasy kit. (Qiagen, Valencia, CA). Multiple PCR reactions were performed to cover the entire HBVgenome obtained from serum and liver of each of the 4 patients with HBV-associated ALF. PCR primers were designed to match the HBV reference sequence V01460 (genotype D, serotype ayw) and used for PCR amplification. PCR products were purified using a MinElute kit (Qiagen, USA). DNA was sheared randomly, processed into a sequencing library using Ion Torrent's Fragment Plus kit and quantified using the Qubit system (Invitrogen). Sequencing libraries were prepared and deep sequencing was performed in an Ion Torrent next-generation sequencer Personal Genome Machine (PGM) as described previously (7). Details on the next-generation sequencing method are reported in the Supplementry Information.

Sequence analysis of HBcAg from chimpanzees with acute hepatitis B. The HBcAg-coding genes were initially amplified from chimpanzees' liver RNA by RT-PCR with 30 cycles of 95^{o}C, 1min, 55^{o}C, 1 min, and 72^{o}C 1min, using the following set of primers, core 5'-1: ATGCAACTTTTTCACCTCTGCCTA, and core 3'-1: CTAACATTGAGATTCCCGAGATTGAGATCT. The first PCR product was used as a template for further amplification by semi-nested PCR with a new 5'-end primer (TTCAAGCCTCCAAGCTGTGCCTTGG) and the same 3'-end primer under the same cycling condition as in the first PCR. The PCR products were purified and cloned into pGEM-T (Promega) vector. To avoid the possibility that mutations were introduced by PCR,

five clones from each chimpanzee were sequenced. Consensus HBcAg-coding sequence was determined only when all five clones showed the same nucleotide sequences. The presence of mutations in the precore region as well as in the core region were identified by comparison with the reference ayw sequence (8), as the two animals were inoculated with HBV, strain ayw.

Cell Culture and Transfection. Human hepatoma cells, HepG2, were maintained in Dulbecco's modified Eagle's medium (DMEM; Invitrogen) supplemented with 10% fetal bovine serum at 37°C and 5% CO_2. The cells were grown to 70-80% confluence in 10-cm-diameter dishes and transfected with DNA by TransIT-2020 (Mirus, Madison, WI). A total of 15 µg of 3.2-kb linear full-length HBV genomic DNA were used to transfect HepG2 cells. To ensure that the same amount of DNA for each construct was used in transfection experiments the concentration of each HBV DNA preparation was determined by spectrophotometer and was confirmed on agarose gel. The culture supernatants and the cells were collected 52-72 h post-transfection, and viral DNA and antigens were quantified. Transfections were conducted at least three times with independently prepared cells and DNA. Production of HBsAg in culture supernatant, as indication of successful transfection, was monitored in each transfection.

Quantification of HBV DNA and HBV RNA in tissue culture by real-time polymerase chain reaction. To remove input HBV DNA, culture supernatants were treated with DNase I (RQ1 RNAse-Free DNAse, Promega # M6101). Total extracellular DNA was then extracted with a QIAamp DNA Blood Mini Kit (Qiagen). For extraction of total intracellular viral DNA, the transfected cells were lysed with RIPA buffer (Sigma), followed by DNaseI treatment. The viral DNA was released from the core particle by proteinase K treatment and purified by phenol/chloroform extraction. The viral DNA was finally precipitated by ethanol and resuspended in TE buffer. Intracellular RNA was extracted

from whole-cell lysates by using the RNeasy Mini Kit (Qiagen), followed by DNaseI treatment. Complementary DNA was synthesized with the ABI High-Capacity cDNA Reverse Transcription Kit (Applied Biosystems #4374967). The levels of extracellular HBV DNA and intracellular HBV DNA and RNA (cDNA) were determined using quantitative real-time polymerase chain reaction, as previously reported (5) and described above in the serum and liver DNA extraction and real-time polymerase chain reaction section.

Quantification of HBsAg and HBcAg expression in tissue culture. The amount of hepatitis B surface antigen (HBsAg) in cell culture supernatants was determined with commercial immunoassays (DiaSorin, Saluggia, Italy), using a US Bureau of Biologics internal reference standard as described previously (9). The amount of HBcAg was quantified by ELISA and immunoprecipitation followed by Western blotting (IP-WB). First, a total of 7 anti-core antibodies were tested for reactivity to wild-type, 241 and 31 core proteins by ELISA and WB (Table S4). As a result, serum IgM from patient 32 and 219, and serum IgG from patient 98 with chronic hepatitis B were found to react with wild-type, 241 and 31 core protein equally well and therefore were selected for the assay. Cells were washed 3 times with PBS at 52-72 h post-transfection and lysed with 1 ml of RIPA buffer (Sigma). The cell lysates were clarified by centrifugation and the supernatant was used for either ELISA or IP-WB. For ELISA, streptavidin-coated plates (ThermoFisher Scientific) were first incubated with biotinylated anti-IgM at 0.1 µg per well for 2 h, followed by incubation with patient 32/219 serum containing anti-HBc IgM for 2 h. After washing, serial 3-fold dilutions of cell lysates from cultures transfected with various HBV DNA or untransfected/vector-transfected controls were added starting from 150 µl of the undiluted lysate, and incubated for 1 h. Captured HBcAg was detected by human anti-HBcAg IgG from P98 serum followed by incubation with HRP-conjugated goat anti-human IgG Fc. Each assay included purified recombinant HBcAg of wild-type-HBV, 31 or 241 as positive controls. Serially 3-fold diluted recombinant HBcAg from the wild-type-HBV, 31 and 241 strains were used to generate linear

standard dose-response curves, which was used to calculate the concentration of HBcAg of wild-type-HBV, 31 or 241 in the cell lysate, respectively (Fig. S2, A and B). The assay was repeated three times and the results were analyzed by unpaired t-test for statistical significance. IP-WB was only performed on samples with ayw and 241 transfections because no antibodies that can react with 31 core protein on WB were available. For IP-WB, the cell lysates (400 µl) of HepG2 transfected with wild-type-HBV, 241 HBV DNA or untransfected HepG2 were incubated with 2 µl of human anti-HBcAg IgM from P32 overnight at 4°C. The IgM-HBcAg complex was captured by protein G beads pre-loaded with goat anti-human IgM. After extensive washing, the beads were resuspended in SDS-PAGE sample buffer and proteins were separated on a 4-12% NUPAGE gel, followed by transfer onto a PVDF membrane. After blocking in 5% milk in PBS for 1 h, the membrane was incubated with human P98 serum containing anti-HBc IgG overnight at 4°C. After washing, the membranes were incubated with HRP-conjugated anti-human IgG Fc for 1 h at room temperature. The blot was developed by incubation of the membrane with Supersignal west dura extended duration substrate (Thermo Scientifc) and exposed to X-ray film.

Generation of full-length replication competent HBV DNA genomes. The synthesized HBV DNA monomers were cloned into pUC57 plasmid at XhoI site. Upon digestion with XhoI restriction enzyme, the full-length HBV genome was released from the vector and used for transfection and subsequent functional analysis. QuickChange Lightning Site-Directed Mutagenesis Kit (Agilent Technologies, La Jolla, CA) was used to introduce G1896A mutation into wild-type ayw HBV genome, resulting in generation of ayw mutant strain containing the precore stop codon. The presence of the mutation was confirmed by DNA sequencing.

Expression of HBsAg in mammalian cells. Based on HBV sequences obtained from each patient with ALF (patient 31, 32, 219 and 241), a 2.2-kb gene fragment corresponding to

nucleotide positions 2705 to 1745 of the HBV coding for S gene promoter 1 and 2, enhancer I and II, and preS1, preS2 and S peptides was synthesized by Gene Art (Invitrogen) in accordance with HBV sequences for each patient with ALF and the published ayw HBV sequence (8). The gene was cloned into pFRT/LacZeo vector at AscI and SacI sites and the construct was verified by sequencing. HepG2 cells were transfected with the construct using TransIT-2020 (Mirus) and then incubated at 37°C, 5% CO_2 for 6 days for expression. The expressed HBsAg in culture supernatant was collected and detected by ELISA using rabbit anti-S polyclonal antibody (Fitzgerald 20-HR20) and mouse anti-S monoclonal antibody (mAb) (Fitzgerald 10-H051). For the ELISA, wells in a 96-well plate were coated with anti-S mAb, followed by addition of culture supernatant and the captured HBsAg was then detected by anti-S polyclonal antibody. HBsAg (available from antibodies-online.com, ABIN622168) was used as positive control. The culture supernatant was concentrated by 10-20-fold using Amicon-100 kD cut (Millipore) and was used for panning a phage Fab library.

Expression and purification of HBV core particles from patients with HBV-associated ALF. Based on sequencing data, genes coding for HBcAg of patient 31, 32, 219 and 241, and the gene coding for wild-type ayw HBcAg (8) were synthesized by Gene Art (Invitrogen). Each HBcAg-encoding gene was cloned into pET14b at NcoI and XhoI sites and was confirmed by sequencing. The *E. coli* of BL21(DE3)pLysS cells were transformed with the recombinant plasmids carrying HBcAg-encoding genes and grown for expression. Briefly, a single bacterial colony was inoculated into 10 ml of LB media and incubated with shaking at 37°C overnight. The overnight culture was transferred into 500 ml of fresh LB and cultured for 2-4 h at 37°C. The expression was induced by addition of IPTG to final concentration of 0.2 mM and the culture continued for additional 4 h. The bacterial cells were collected by centrifugation at 5000xg for 15 min, resuspended in 40 ml of 1X PBS, and lysed through three cycles of freeze/thaw. The HBV core particles in the supernatant following centrifugation were precipitated by addition of ammonium sulfate to final 25% saturation and incubation

with rotation at 4°C for 2h. The pellet was collected by centrifugation and resuspended in 3 ml of 1x PBS. The HBV core particles were finally purified by ultracentrifugation on 15-45% sucrose gradient, buffer-exchanged and concentrated in 1X PBS by ultrafiltration with MW cutoff of 100 kD and sterilized by filtration through 0.22 μm filter. The purity and concentration of HBV core particles were estimated by SDS-PAGE along with known concentration of commercial available HBV core protein and the identity was confirmed by reaction with polyclonal anti-HBc on enzyme-linked immunoassay (ELISA).

Kinetics analysis of HBcAg expression in cell culture. Linear full-length replication-competent HBV DNA of ayw, 31 and 241 were generated by XhoI digestion and used for transfection. HepG2 cells were maintained in DMEM supplemented with 5% fetal bovine serum at 37°C and 5% CO_2. The cells were grown to 70-80% confluence in 5-cm-diameter dishes and transfected with DNA by TransIT-2020 (Mirus, Madison, WI). A total of 5 μg of 3.2-kb linear full-length HBV genomic DNA was used to transfect HepG2 cells. The cells were collected on day 1, 3 and 5, respectively after transfection, and HBcAg was quantified by ELISA as described before. Transfection experiments were repeated at least two times with independently prepared cells and DNA. The production of HBsAg in culture supernatant, as indication of successful transfection, was monitored in each transfection.

Immunofluorescence, confocal microscopy and imaging analysis. HepG2 cells were transfected with full-length, replication-competent linear HBV DNA of wild-type HBV strain (ayw) or one of two ALF-variants (HBV-31, HBV-241) and cultured for 48 h. The transfected HepG2 cells were fixed with 4% formaldehyde in PBS for 15 minutes at room temperature, followed by 3 washes with 1XPBS. Cells were also fixed and permeabilized with 0.5% Triton X-100 for 5 minutes at room temperature. Both fixed only and fixed plus permeabilized cells were blocked with 5% BSA, 2% goat serum in PBS for 1 h at room temperature, followed by incubation with primary antibodies; human anti-HBcAg C7 (isolated

from an ALF patient) (1µg/ml) and anti-HBsAg (Abcam) (1:3) for 2h at room temperature. After washing three times with 1XPBS, Alexa-488 or Alexa-594 conjugated secondary antibodies (Invitrogen) (1:500) were applied for 1 h at room temperature, and then cells were washed again three times with 1XPBS. Finally, cells were incubated briefly (5 min) with 0.3 mM DAPI (4', 6'-diamidino-2-phenylindole) and were washed once with 1XPBS. Slides were mounted in Prolong Gold (Invitrogen).

Images were obtained using a Leica SP5 X-WLL laser scanning confocal imaging system (Leica Microsystems, Exton, PA, USA) equipped with the 40X (NA 1.25) and 63X (NA 1.4) oil immersion objectives. DAPI was excited using UV 405 laser, rest of the fluorophores were excited with a white light laser with a range of wavelengths (470-670nm). Differential interference contrast (DIC) imaging technique was used to retrofit fluorescence images in order to show localization of the fluorescent signal on the plasma membrane and inside the cells. To avoid emission crosstalk, sequential frame averaged scans were set up for each fluorophore and DIC. Data were deconvolved using Huygens Professional software (version 18.04.0-p5, Scientific Volume Imaging BV, Hilversum, Netherlands) and images were exported using Imaris software (version 9.2.0, Bitplane AG, Zurich, Switzerland).

Cell surface binding of HBcAg and complement fixation. HepG2 cells were seeded in a 6-well plate with cover slips at 60% confluence. After culture for 2 days at 37^{o}C, 5% CO_2 in DMEM with 10%FBS, the cells were washed twice with cold PBS. A recombinant HBcAg derived from wild-type HBV (ayw) or ALF-HBV (31 or 241) at a concentration of 10 µg/mL in PBS containing 10% FBS were added into separate wells. Wells with no HBcAg, but PBS containing 10% FBS served as negative controls. The plate was incubated on ice for 1 h followed by 5-minute washes with cold PBS. The plate was subsequently incubated with 1µg/ml of anti-core Fab E3 conjugated with Alexa-647 (cloned from the liver of an ALF patient) in PBS/10%FBS on ice for 1 h. Following 3 washes with cold PBS, cells were fixed

with 4% formaldehyde in PBS for 15 minutes at room temperature. Finally, cells were washed, stained with DAPI, mounted on slides and examined using confocal microscopy.

Flow cytometry analysis was also used to examine the binding of HBcAg to the cellular membrane. Single-cell suspensions of HepG2 cells were incubated with LIVE/DEAD fixable Aqua dead cell stain (Invitrogen, ref. L34957) to assess their viability. After washing with FACS Buffer (2% FBS in PBS), the cells were incubated at 4 °C with 10 µg/ml HBcAg derived from HBV wild-type (ayw), HBV-31 or HBV-241 in 500 µl PBS/2% FBS for 1 hour. In the binding assay, HBcAg particles were detected using Alexa 647-conjugated HBcAg-specific Fab E3. In the complement-fixation experiment, the cells were further incubated at 4°C with 1 µg/ml human anti-HBcAg (IgG1C7) in 500 µl PBS/2% FBS for 1 hour, followed by incubation with 2.8 µg/ml C1q purified protein (Complement Technology Inc.) for an additional hour. Then, the cells were washed and stained with rabbit anti-C1q FITC antibody (Abcam, ref. ab4223). Finally, the cells were fixed and permeabilized using BD Cytofix/Cytoperm Kit (Becton Dickinson). Samples were analyzed on a CANTO-II flow cytometer (Becton Dickinson) and FlowJo v10 software. At least 30,000 live cells were counted per sample, and the median fluorescence intensity (MFI) was determined. Threshold levels were set according to the negative control. Fold changes were calculated by dividing the MFI value of the sample by the value of the negative control. In the complement-mediated cell-lysis experiment, after the formation of the immune complexes witht the anti-HBcAg human antibody IgG 1C7 the cells were incubated for 1 hour at 37°C in the presence of complete serum diluted 1:400 in PBS. Then, the cells were stained with propidium iodide and analyzed within 1 hour on a CANTO-II flow cytometer; at least 10,000 cells were counted per sample, and the percent of propidium iodide-positive cells was determined. The threshold levels were set according to the negative control (cells treated with complete or C3-depleted serum in the absence of immune complexes).

Immunohistochemistry. Formalin-fixed paraffin-embedded liver sections obtained from each patient with ALF were used to perform immunohistochemical staining using a panel of antibodies including CD3, CD8, CD20, CD68, CD163, IgM, IgG, Kappa, Lambda, Mum-1, C1q, HBsAg, HBcAg (Dako), CD4, CD138 (AbD Serotec). We also used CD8 (Leica Biosystems) and CD163 (Thermo Scientific). Briefly, sections of 3 to 5 μm were deparaffinized through graded alcohols and xylene. Immunohistochemical stainings were performed after antigen retrieval using either citrate buffer (10 mmol, pH 6.0) or EDTA (1 mmol, pH 9.0). Slides were incubated in Tris-goat serum (3%) for 15 min and then incubated at room temperature with primary antibodies. Detection was carried out on the automated system BenchMark XT autostainer (Ventana Medical Systems) or Bond RX (Leica Biosystems) platform according to the manufacturer-supplied protocols. Formalin-fixed liver sections obtained from two chimpanzees (Ch. 5835 and Ch.1627) at three time-points during the course of acute self-limited hepatitis B were stained using the same panel of antibodies as used for human tissue.

Gene-expression profiling and statistical analysis. Gene-expression profiling was performed on messenger RNA (mRNA) in all 17 liver specimens obtained from the four patients with ALF and in all 17 controls, using Affymetrix Human U133 Plus 2 arrays (Affymetrix, Santa Clara, CA), containing 54,675 probe sets representing approximately 38,500 human genes, as previously reported (10). MicroRNA-expression profiling was performed on 13 liver specimens, including 2 liver specimens for patient 241, 3 for patient 31, 5 for patient 219 and 3 for patient 32, and in 17 liver specimens of the control group, using Affymetrix GeneChip miRNA 2.0 arrays (Affymetrix), which contain 1,121 pre-microRNA (mir-), and 1,105 mature microRNA (miR-) probe sets, as previously reported (11). As Affymetrix IDs, originally referred to miRBASE 15, differ from the latest miRBase 21 nomenclature (http://www.mirbase.org/) a synopsis of original Affymetrics IDs and miRBase 21 IDs is shown in table S8. False miRNAs removed from miRBase 21 were also excluded

from the study. RNA was extracted from frozen liver specimens using the miRNeasy Mini Kit (Qiagen). Total RNA (500 ng), including microRNA, was poly(A) tailed and then directly ligated to a fluorescent dendrimer (a branched single and double stranded DNA molecule conjugated to biotin) using the FlashTag Biotin HSR RNA Labeling Kit (Affymetrix). An ELOSA was performed prior to hybridization and analysis of the arrays in order to verify that all miRNAs were correctly labeled with the biotin molecule at the 3' end. All samples passed the quality control (QC) assessment performed with the miRNA QCTool available through Affymetrix, using chip-specific quality control probes. RNA quality and integrity was assessed with the RNA 6000 Nano Assay on the Agilent 2100 Bioanalyzer (Agilent Technologies, Santa Clara, CA). Raw microarray data (cel files) were imported into BRB-ArrayTools (linus.nci.nih.gov/BRB-ArrayTools). Probe set summaries were computed using the RMA algorithm. Multiple transcripts of the same gene were averaged, whereas transcripts of unknown genes were discarded. For the comparison between ALF and control livers, multiple specimens obtained from the same liver were averaged. MicroRNA and mRNA differentially expressed in ALF were identified by a multivariate permutation F-test with a maximum false discovery rate of 1 % with 80 % confidence level, using BRB-ArrayTools (12). Principal component analysis was obtained using Multibase (www.numericaldynamics.com). Statistical analyses were done with $\log_2$-transformed data. Fold changes were calculated as the ratio between the geometric means of ALF livers and normal livers. To ensure a robust analysis, only mRNAs with absolute fold changes >3 were selected for the analysis. Functional data were obtained from IPA (Ingenuity® Systems, www.ingenuity.com).

Screening of Fab-display phage libraries. Phage libraries of IgG1 and IgM Fab were panned separately by solid-phase selection on ELISA plates coated with homologous or wild-type HBsAg and HBcAg. For HBcAg panning, wells of 96-well plate were coated with 100 µL /well of solution of 5 µg/ml antigen in 1x PBS. For HBsAg panning, wells of 96-well plate

were coated with 100 µL /well of 5 µg/ml of anti-S monoclonal antibody and the coated antibody was used to capture HBsAg following addition of 100 µL of concentrated culture supernatant. Wells were incubated overnight at 4ºC and blocked with 3% milk in 1x PBS. Phage Fab suspensions containing 10^{12} pfu in 100 µL 1x PBS with 2% milk were added and incubated for 2 h at room temperature. After incubation, phages were aspirated, the wells were washed, and bound phages were eluted, titrated, and replicated as described (13). After three rounds of panning, 96 randomly picked single phage-Fab clones from each library were screened for specific binding to the respective antigen by phage ELISA as described (9).

Analysis of intrahepatic IgM and IgG extracted from liver tissues of ALF patients. Frozen liver tissue obtained from two patients with HBV-ALF and from a control liver donor, negative for HBV markers with normal liver pathology, were homogenized in 1 ml of 1XPBS. The extracts were incubated at 37ºC for 10 min after adding urea to final concentration of 5M, and then centrifuged for 10 min at 15,000xg. The supernatants were collected and dialyzed overnight against 1XPBS. The total protein concentration in each liver tissue extract was measured by BCA (ThermoFisher Scientific) and used for normalization. Total and core specific IgM and IgG were quantified by ELISA along with commercially available IgM and IgG with known concentration as positive controls. A total of 100 µl of goat-anti-human IgM or IgG at 4 µg/ml were coated in each well of a 96-well plate. After blocking with 3% milk in 1XPBS and washing, 100 µl of liver extract and seven 3-fold serial dilutions were added to each well. Seven 3-fold serial dilutions of commercially available IgM and IgG starting with 3 µg/ml were also included as standard curves. The captured IgM or IgG was detected by HRP-conjugated monoclonal anti-human IgM or anti-IgG, respectively. The reaction was developed by adding tetramethylbenzidine (TMB) and stopped by adding sulfuric acid, and the intensity was measured using an ELISA reader at OD_{450}. A linear standard curve was made for the control IgM or IgG antibodies, from which the concentration of IgM and IgG extracted from the liver was calculated. The final concentration

of IgM and IgG from each sample was normalized as amount of IgM and IgG per microgram of total protein. The antibody titers of core-specific IgM and IgG were determined by ELISA. For core-specific IgM, 100 µl of goat anti-human IgM at 4 µg/ml were added into each well in a 96-well plate. After blocking and washing, the liver extract and its 3-fold serial dilution were added into each well from top to the bottom, followed by adding 3 recombinant HBcAg, ayw, 219 and 241 at 5 µg/ml for each sample. The captured HBcAg was detected by anti-HBc positive serum from a patient with chronic hepatitis B and then revealed by HRP-conjugated monoclonal anti-human IgG. For titration of core-specific IgG, 100 µl of goat anti-human IgG at 4 µg/ml were added into each well of a 96-well plate. After blocking and washing, 3-fold serial dilutions of the liver extracts were added into each well, followed by washing and addition of recombinant HBcAg (ayw, 219 and 241) at 5 µg/ml. Captured HBcAg was detected using serum from ALF patient 241 and subsequently by HRP-conjugated monoclonal anti-human IgM. The reaction was developed as above with TMB. The nonspecific IgM and IgG were used in each plate for negative controls. All OD_{450} values were subtracted by the OD_{450} value from the negative controls. The last sample dilution that reached OD450 value >0.2 was regarded as antibody titer (OD value for the negative control was around 0.045). The titer was normalized based on the total protein, whereby each sample was adjusted to the same amount of total protein.

Affinity measurement by SPR. HBS-EP buffer (10 mM HEPES pH 7.4, 150 mM NaCl, 3.4 mM EDTA, 0.005% surfactant P20) was used as the working buffer for all SPR binding experiments. Buffers and reagents for amine coupling (n-(3-dimethylaminopropyl)-n'-ethylcarbodiimide hydrochloride, n-hydroxysuccinimide, and acetate buffers) as well as sensor chips CM5 were acquired from Biacore, GE Healthcare (Piscataway, NJ). SPR experiments were performed in a Biacore 3000 instrument (GE Healthcare, Piscataway, NJ) at 25 °C. Antigens were coupled to the sensor surface of CM5 chip by standard amine coupling (14). Immobilization was achieved with 100 µg/mL protein in sodium acetate buffer at pH 4.5

using a flow rate of 5 µL/min. The target immobilization level of antigen of ~1000 RU was obtained by adjusting the reaction time. For each sensor chip, a reference surface was prepared by activating the surface followed by mock derivatization without injecting antigen. For binding affinity analyses, a series of 7 concentrations (0.3 – 500 nM) of each Fab molecule was injected across the sensor surface at a flow rate of 5 µL/min. The time-course of the binding signal was observed for 1,200 sec, followed by 3,600 sec observation of dissociation during buffer wash. If the signal at the end of this period has not returned to baseline level, a regeneration step with 5µL injection of NaOH solution (5 – 25 mM) was used to break the remaining binding, which caused the signal to return to baseline. SPR binding data were first processed in BIAevaluation (version 4.0.1, Biacore GE Healthcare, Piscataway, NJ) in order to subtract reference signals including both the signal from the reference cell and the background signal observed in blank buffer injections. The processed data were then exported into Microsoft Excel and saved as an .xls file, which is used as the input file for binding analysis in the software EVILFIT (https://www.youtube.com/watch?v=QXkXTN0gwck) using the surface site distribution model as previously described in detail (15). Briefly, the kinetic traces of all the concentrations of the Fab molecule binding to the immobilized antigen under study were globally fitted for continuous distributions of equilibrium binding constants (K_d) and dissociation rate constants (k_{off}). In the resulting site distribution plot, the main peaks were integrated to calculate the average K_d and k_{off} values corresponding to the observed binding events.

Next-generation sequencing of intrahepatic IgM and IgG repertoire and bioinformatics analysis of Illumina paired-end sequencing. To amplify genes coding for Fd (VH + CH1) we used the same set of 5'-end VH family specific primers and 3'-end IgM-or IgG1-specific CH1 primer that we previously used in the construction of the phage display library. A total of 10 amplicons were generated, including IgM and IgG from

liver RNA extracted from ALF-Patient 31, 241, 32, 219 as well as from a liver donor with histologically normal liver (donor 37) that was negative for markers of HBV infection. The amplicons were purified and subjected to Illumina 2X300 bp paired-end sequencing and analyzed (details are provided in the supplementary information). Briefly, Illumina adapters were added to 30 ng of amplicon DNA using the Ovation Ultralow System V2 1-96 kit (NuGen Technologies, Inc.). Amplicons were pooled in an equal volume ratio. An aliquot of the pool was run on a MiSeq (Illumina, Inc.) using a MiSeq Reagent Nano kit, ver2. This QC run consisted of 25 cycles followed by an index read. The pool was then rebalanced based on the percentage of reads seen for each amplicon's indexes. The final pool was then sequenced on the HiSeq 2500 in Rapid mode using version 2 chemistry to generate a minimum of 9 M paired-end 300 base reads per amplicon. Post-run processing of data was performed using RTA 1.18.64 and CASAVA 1.8.2. Paired-end Illumina sequencing reads were merged using FLASH (Fast Length Adjustment of SHort reads) (16). Primer sequences were removed using FLEXBAR with 0.3 threshod (17). The Stand-alone IGBLAST (18) running on the NIH HPC Biowulf Linux cluster (https://hpc.nih.gov/) was used for V(D)J germline gene assignments, and an in-house developed python script was applied to process IGBLAST outputs (19). Non-Ig, non-duplicate and non-production reads were filtered out. Reads containing stop codon and Phred scores of less than 20 occurring over 80% of the V(D)J region were also discarded from all NGS samples. Only sequences assigned FR1-FR4 were retained in the data set. Unique antibody sequences were extracted from reads passing the steps above and were subjected to further analysis. The first nucleotide of the second conserved cysteine codon of the V region was used to evaluate somatic hypermutations. Antibody sequences with equal or less than 1% mutations were considered to be in germline configuration. Antibody sequences shared between IgG and IgM were evaluated at the V(D)J region. For the total reads of high affinity antibodies in NGS samples, we used the V, J germline gene and amino acid sequence of CDRH3 as a filter to extract reads from NGS samples, and more than three mutations on the V germline region were removed. Matplotlib plotting library was used to draw the

corresponding figures. Only reads that had at least two identical sequences at the nucleotide level over the entire V(D)J region were defined as duplicate reads and used for further analysis, including VDJ assignment. The prevalence of high affinity anti-core antibodies in the liver of ALF patients was assessed in the entire IgG and IgM repertoire by using two methods. The first method was based on the quantification of duplicate reads, which are defined as NGS reads that are 100% identical to each other at the nucleotide level over the entire V(D)J region. Thus, the prevalence of a particular sequence using this method was quantified by the total number of duplicate reads that that differ by $\leq 1\%$ at the nucleotide level from that particular sequence normalized by the total number of duplicate reads. The second method was based on the quantification of unique duplicate sequences. Unique duplicate sequences are the set of individual sequences, none of which are identical to each other but for which at least two 100% identical NGS reads of each sequence have been identified. The prevalence of a particular sequence quantified by the unique duplicate sequences method would be the total number of individual sequences that differ by $\leq 1\%$ at the nucleotide level from that particular sequence, normalized by the total number of unique duplicate sequences.

References and Notes

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Supplementary Figures

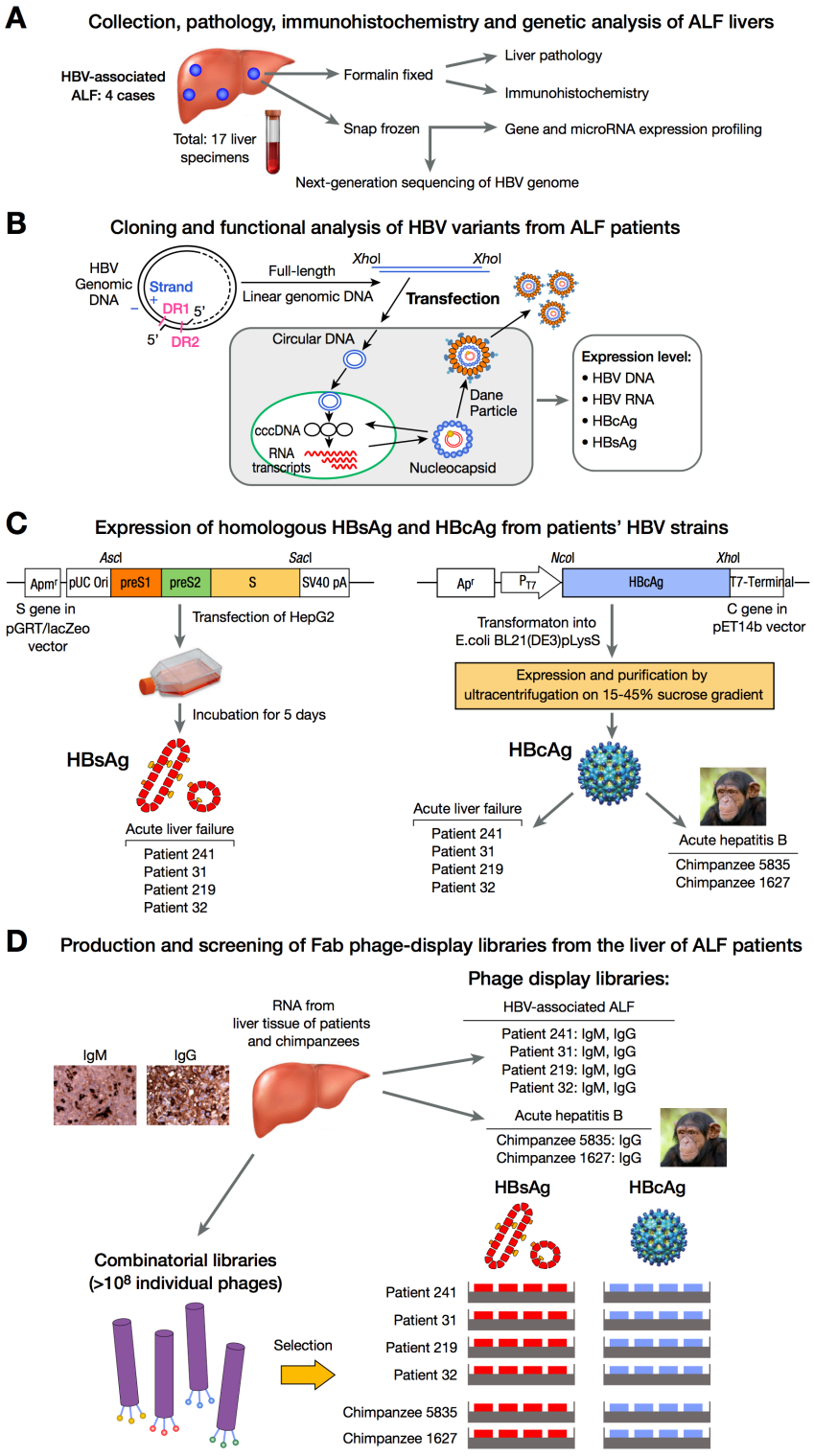


Fig. S1. Study design. (A) At the time of liver transplantation, we obtained serum and 4 or 5 liver specimens from each of the 4 patients with ALF. Each liver specimen was divided into two pieces: one was formalin-fixed and paraffin-embedded and the other was snap frozen. Fixed liver tissue was used for pathological examination and immunohistochemistry. Snap-frozen samples were stored at -80 °C for molecular studies, including mRNA and microRNA expression profiling, next-generation sequencing, and phage-display library. Liver gene and microRNA expression profiling was performed on multiple liver specimens from each patient with ALF and from controls with normal liver. Full genome HBV next-generation sequencing was performed both on serum and liver of each patient with ALF. (B) Linear full-length HBV genomic DNA with XhoI adhesive sites at both terminal ends was transfected into human hepatoma cells HepG2 (20). Upon transfection, the HBV replication cycle from the nuclear generation of viable cccDNA to the final production of infectious viral particles was fully recapitulated; (21) the expression level of viral DNA and RNA and viral proteins was determined following transfection. (C) Based on HBV sequences obtained from each patient with ALF, 2.2-kb gene fragments corresponding to nucleotides 2705 to 1745 of HBV and containing the entire preS1/preS2/S genomic region were synthesized and expressed in HepG2 cells. Likewise, 552 Kb gene fragments corresponding to nucleotides 1901 to 2451, including the gene coding for HBcAg from each ALF patient and from two chimpanzees with acute self-limited hepatitis were synthesized and expressed in *E. coli.* (D*)* Eight phage-display Fab libraries from patients with ALF, one IgG1 and one IgM from each patient, and one IgG1 phage display Fab library from each of the two chimpanzees with acute self-limited hepatitis were constructed using total RNA extracted from liver tissue. No IgM library was constructed from the two chimpanzees because PCR amplification of immunoglobulin μ-chains was negative. The average size of each library was 1×10^8 individual clones. For screening of the libraries, the IgG1 and IgM Fab libraries were separately panned by solid-phase selection by ELISA against the homologous or wild-type HBsAg and HBcAg.

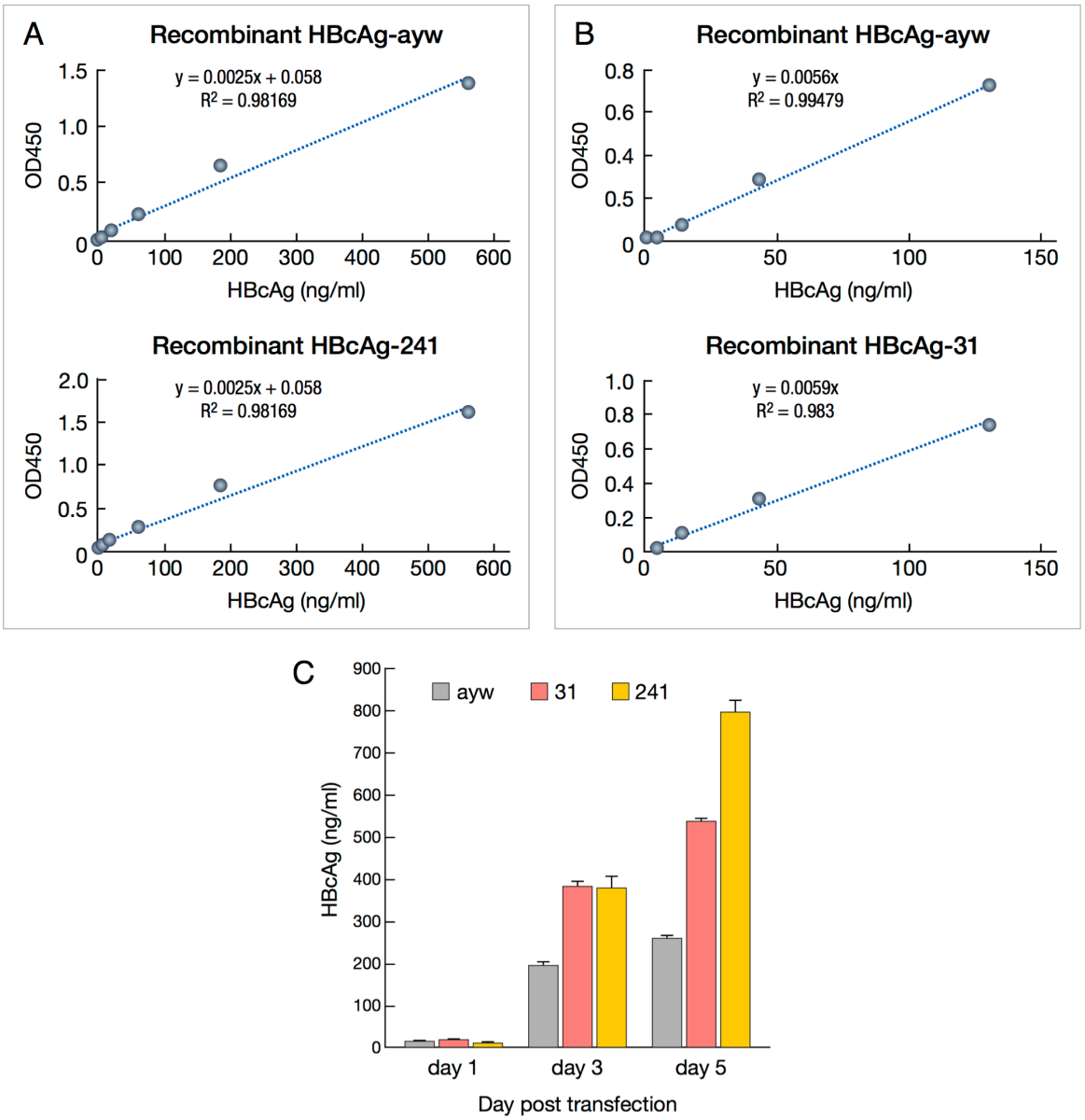


Fig. S2. Standard linear dose-response curves for recombinant HBcAg derived from ayw, 31 and 241 respectively, and kinetics of HBcAg expression in vitro. (A) Standard curves were used to calculate the concentration of HBcAg from ayw and 241. (B) Standard curves were used to calculate the concentration of HBcAg from ayw and 31. (C) A linear full-length replication-competent HBV DNA of ayw, 31 or 241 was transfected into HepG2 cells. The cells were collected on day 1, 3 and 5 post-transfection, and the core antigens were quantified by ELISA as described in the Methods section. Data are shown as mean ± SE from two transfection experiments with independently prepared cells and DNA.

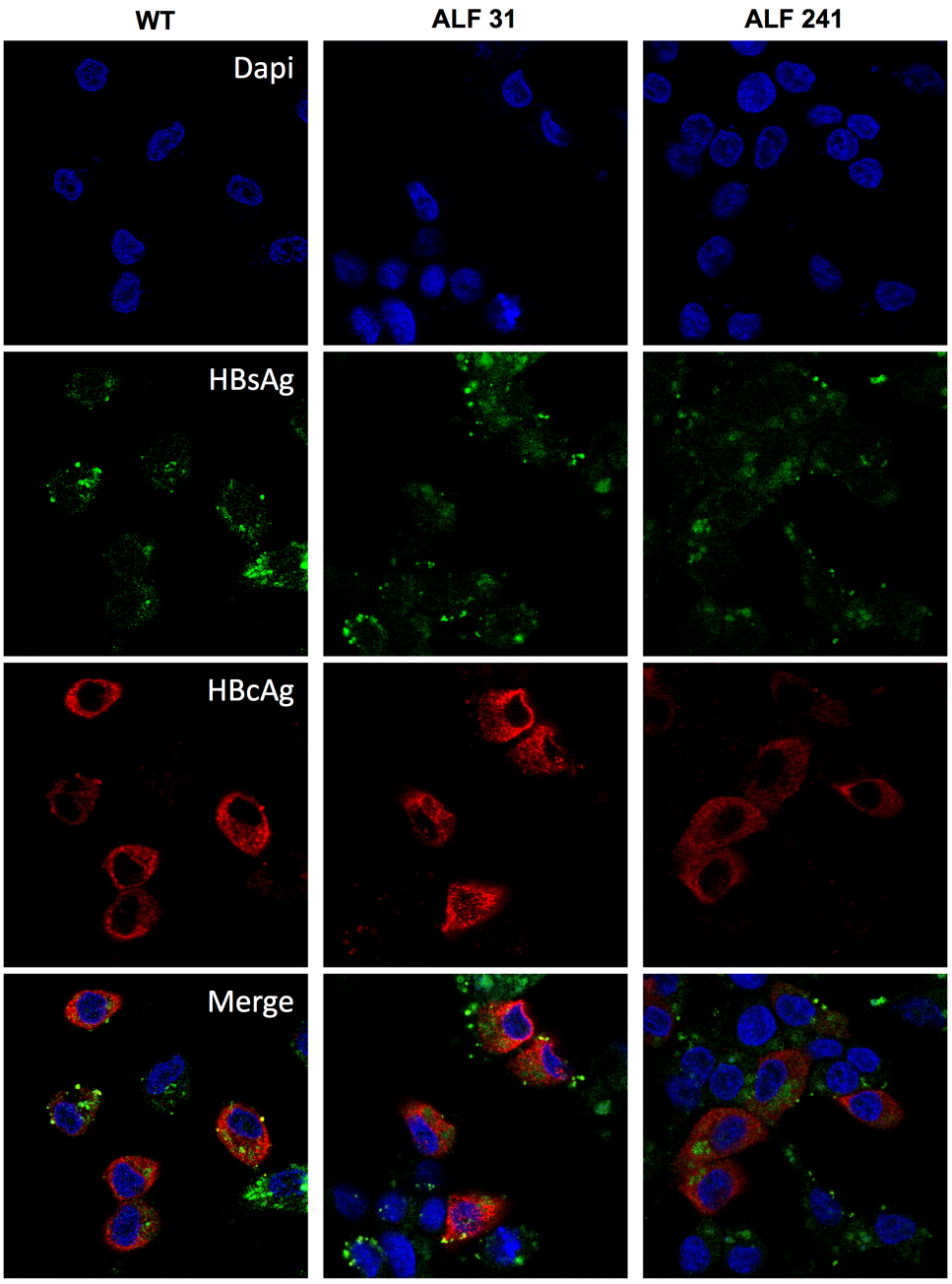


Fig. S3. Intracellular localization of hepatitis B surface antigen (HBsAg) and hepatitis B core antigen (HBcAg) in HepG2 cells analyzed by confocal microscopy. HepG2 cells were transfected with full-length , replication-competent linear DNA of wild-type HBV (ayw) or of two HBV strains derived from two representative patients with acute liver failure (ALF, Patients 31 and 241) and 48 hours later were fixed with paraformaldehyde. Nuclei are shown in blue (Dapi) ; HBsAg appears in green (Alexa 488) and HBcAg in red (Alexa 594). HBcAg staining is very intense in the cytoplasm of all HBV strains. Merged images are also shown at the bottom. Images are visualized at 63X magnification.

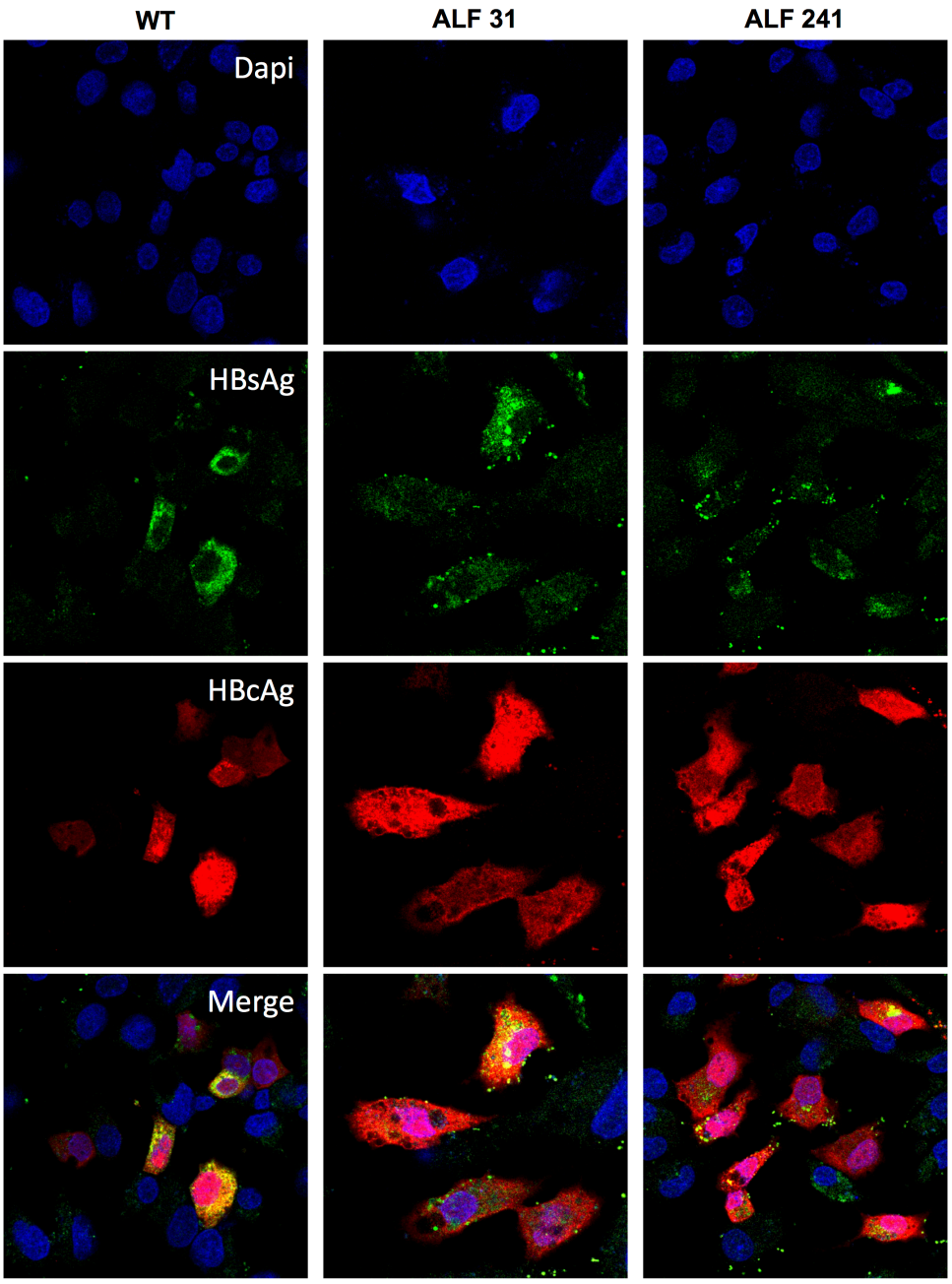


Fig. S4. Intracellular localization of hepatitis B surface antigen (HBsAg) and hepatitis B core antigen (HBcAg) in HepG2 cells analyzed by confocal microscopy. HepG2 cells were transfected with full-length, replication-competent linear DNA of wild-type HBV (ayw) or two HBV strains derived from two representative patients with acute liver failure (ALF, Patients 31 and 241) and 48 hours later were fixed, permeabilized and immunostained by indirect immunofluorescence. HBsAg appears in green (Alexa 488) and HBcAg in red (Alexa 594); nuclei are shown in blue (Dapi). Differential interference contrast (DIC) was used to show localization of the fluorescent signal on the plasma membrane and inside the cells. Merged images are shown at the bottom.

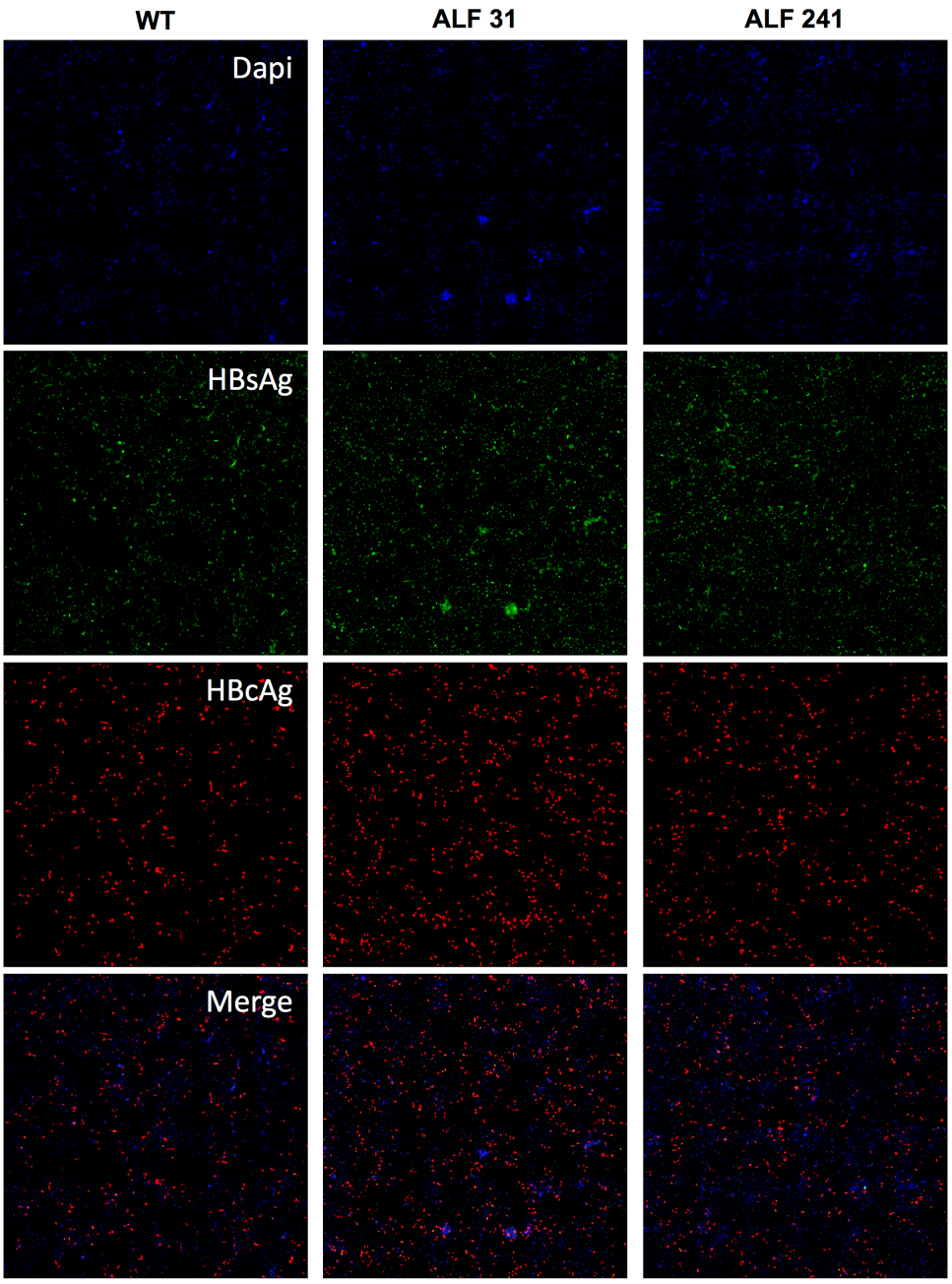


Fig. S5. Intracellular localization of hepatitis B surface antigen (HBsAg) and hepatitis B core antigen (HBcAg) in HepG2 cells analyzed by confocal microscopy. HepG2 cells were transfected with full-length, replication-competent linear DNA of wild-type HBV (ayw) or of two HBV strains derived from two representative patients with acute liver failure (ALF, Patients 31 and 241) and 48 hours later were fixed, permeabilized and immunostained by indirect immunofluorescence. Nuclei are shown in blue (Dapi); HBsAg appears in green (Alexa 488) and HBcAg in red (Alexa 594). Merged images are also shown at the bottom. The cells were visualized at low magnification (10X).

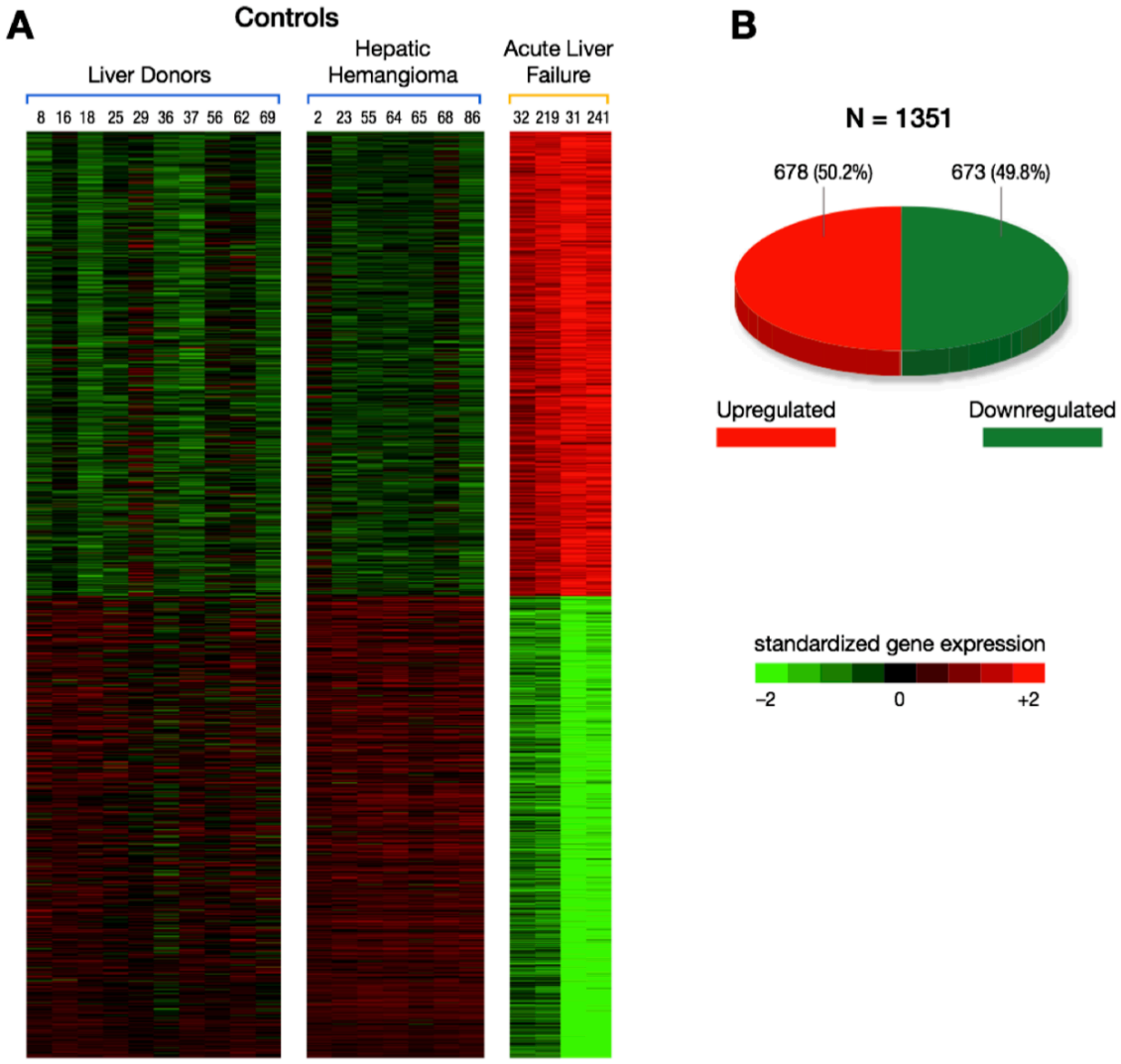


Fig. S6. Heatmap of genes differentially expressed between patients with acute liver failure and controls. (A) Heatmap of the 1,351 genes with a fold change greater than 3 differentially expressed between the four patients with acute liver failure and 17 controls, including 10 liver donors and 7 patients who underwent liver resection for hepatic hemangioma. Each column represents a single patient. Gene expression levels were log2-transformed and row-wise standardized. Up-regulated genes are shown in shades of red, down-regulated genes in shades of green. A gene expression gradient is evident between the two patients with massive necrosis (Patient 241 and 31) and the two with submassive necrosis (Patient 219 and 32). (B) Approximately half of the 1351 differentially expressed genes were upregulated and half downregulated.

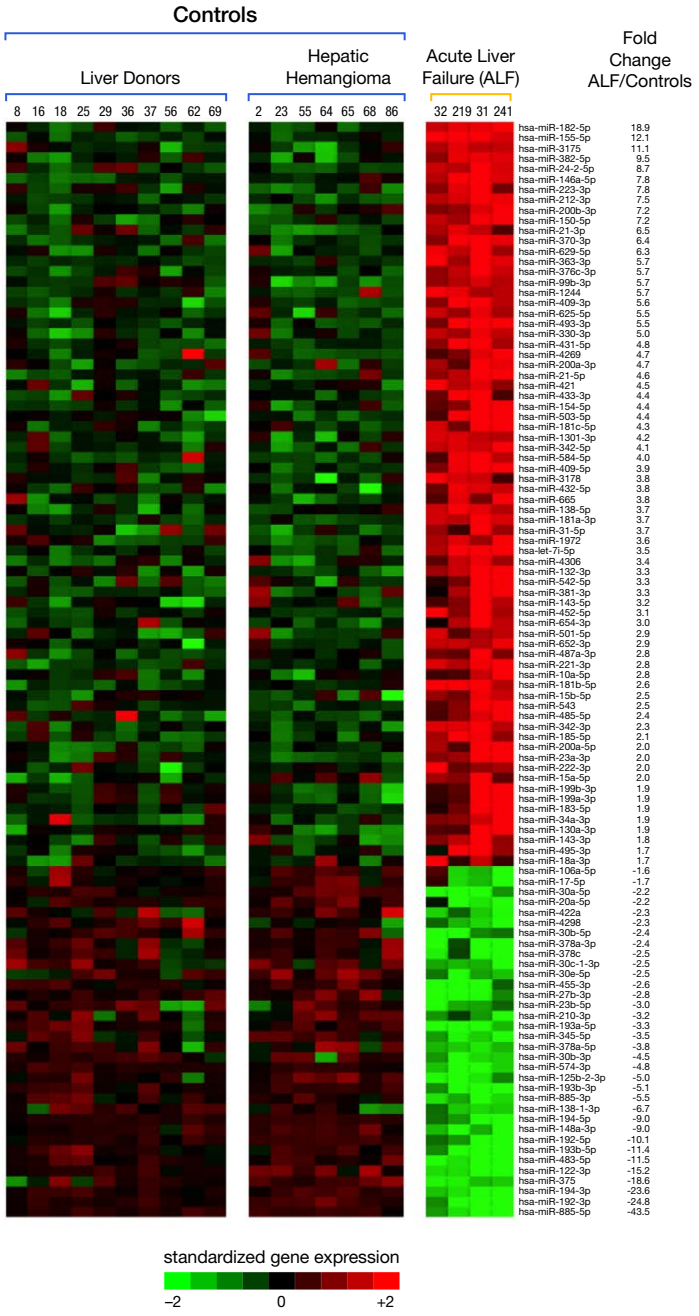


Fig. S7. Heatmap of microRNA differentially expressed between patients with acute liver failure and controls. Heatmap of mature microRNA differentially expressed between the four patients with acute liver failure and 17 controls. Each column represents a single patient. MicroRNA expression levels were log2-transformed and row-wise standardized. Up-regulated microRNAs are shown in shades of red, down-regulated genes in shades of green. Fold changes in expression between acute liver failure patients and controls are shown in the right column.

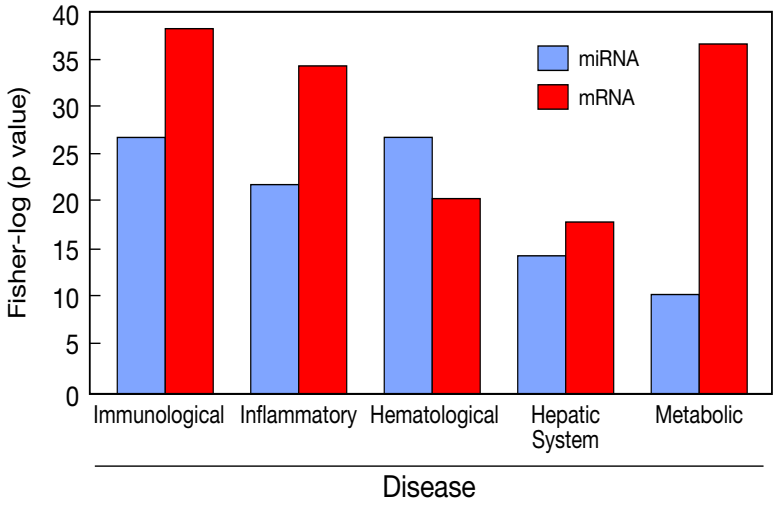


Fig. S8. Major disease categories significantly associated with mRNAs and miRNAs that were differentially expressed in patients with acute liver failure. The analysis shows a predominant immunological and inflammatory disease signature in acute liver failure. Except for metabolic diseases, a consistent correlation of mRNA and miRNA expressions is also evident.

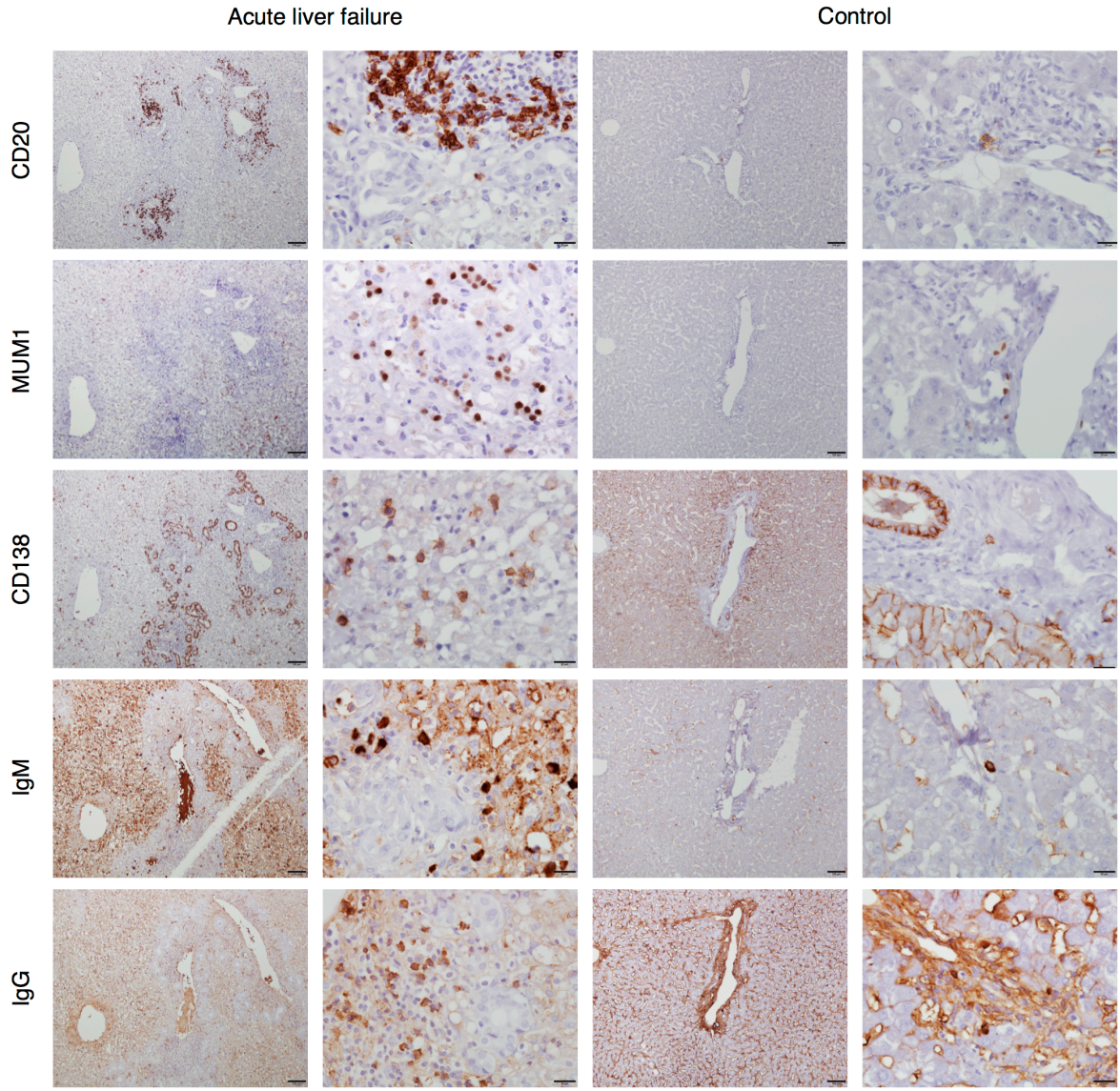


Fig. S9. Continued on the next page.

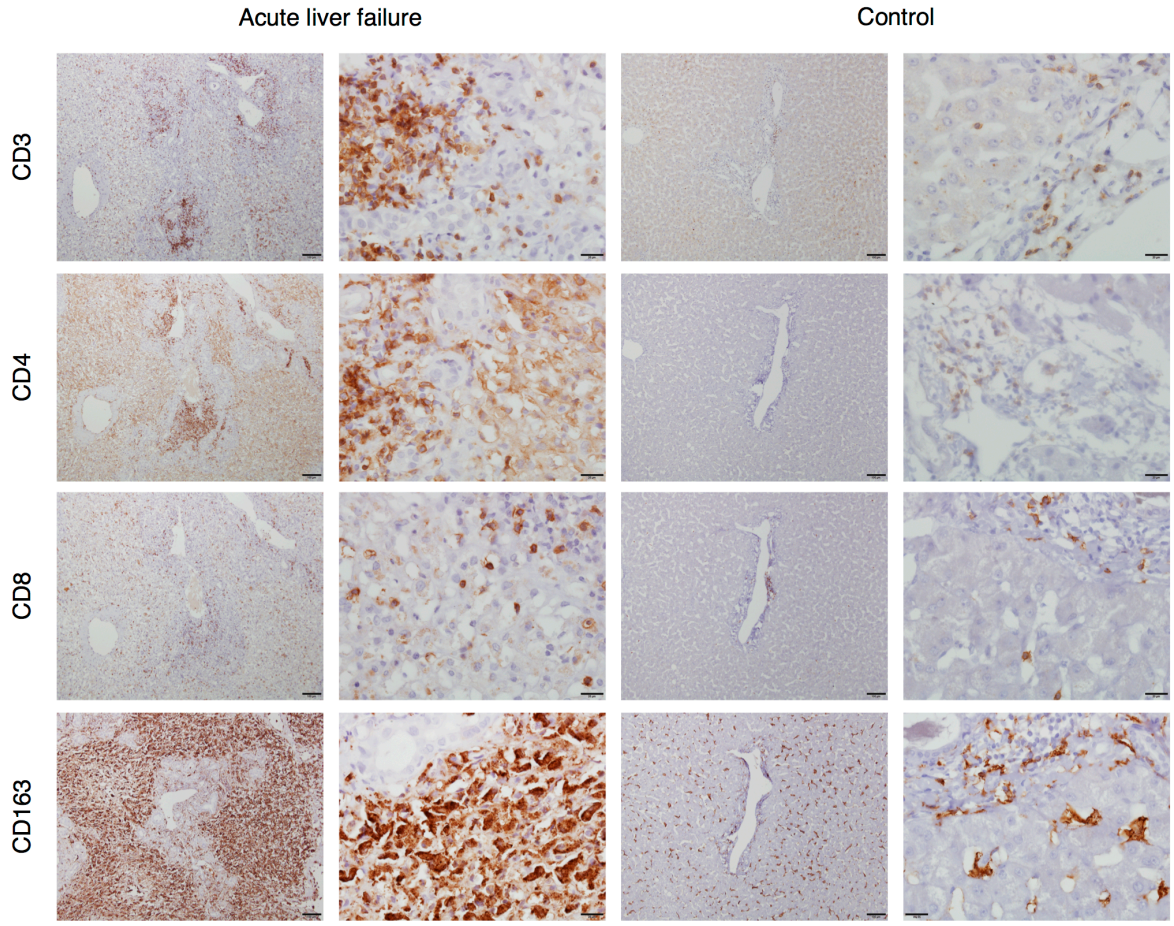


Fig. S9. Immunohistochemical staining of B-cell and T-cell lineage in liver tissue of a representative patient with massive hepatic necrosis at the time of liver transplantation, and of a representative control liver donor. Liver sections were stained with monoclonal antibodies against CD 20, MUM1/IRF4, CD138, IgM, IgG, CD3, CD4, CD8, and CD163. Images of liver sections at different magnification (left columns, 10X; right columns, 100X) show clusters of B cells in the portal tracts and single cells within the lobules. A strong nuclear staining for MUM1/IRF4 is seen in plasmacytoid cells and plasma cells, which extensively infiltrated the lobules. Plasma cells were also strongly positive for CD138, which stains the membrane and the cytoplasm. Positive staining for IgM-secreting mature plasma cells is seen predominantly within the lobules. A diffuse staining is also seen for IgG-secreting plasma cells. Staining for T-cell lineage markers show extensive infiltration of CD3-positive CD8-positive cells and few dispersed CD4-positive cells. Low level diffuse CD4 staining reflects the extensive tissue infiltration by macrophages. Staining for CD163 shows a massive infiltration of the liver tissue by macrophages. Sections from the control liver show only rare cells expressing B-cell and T-cell markers. Positive staining for CD163, IgM and IgG was limited and almost confined to the sinusoids.

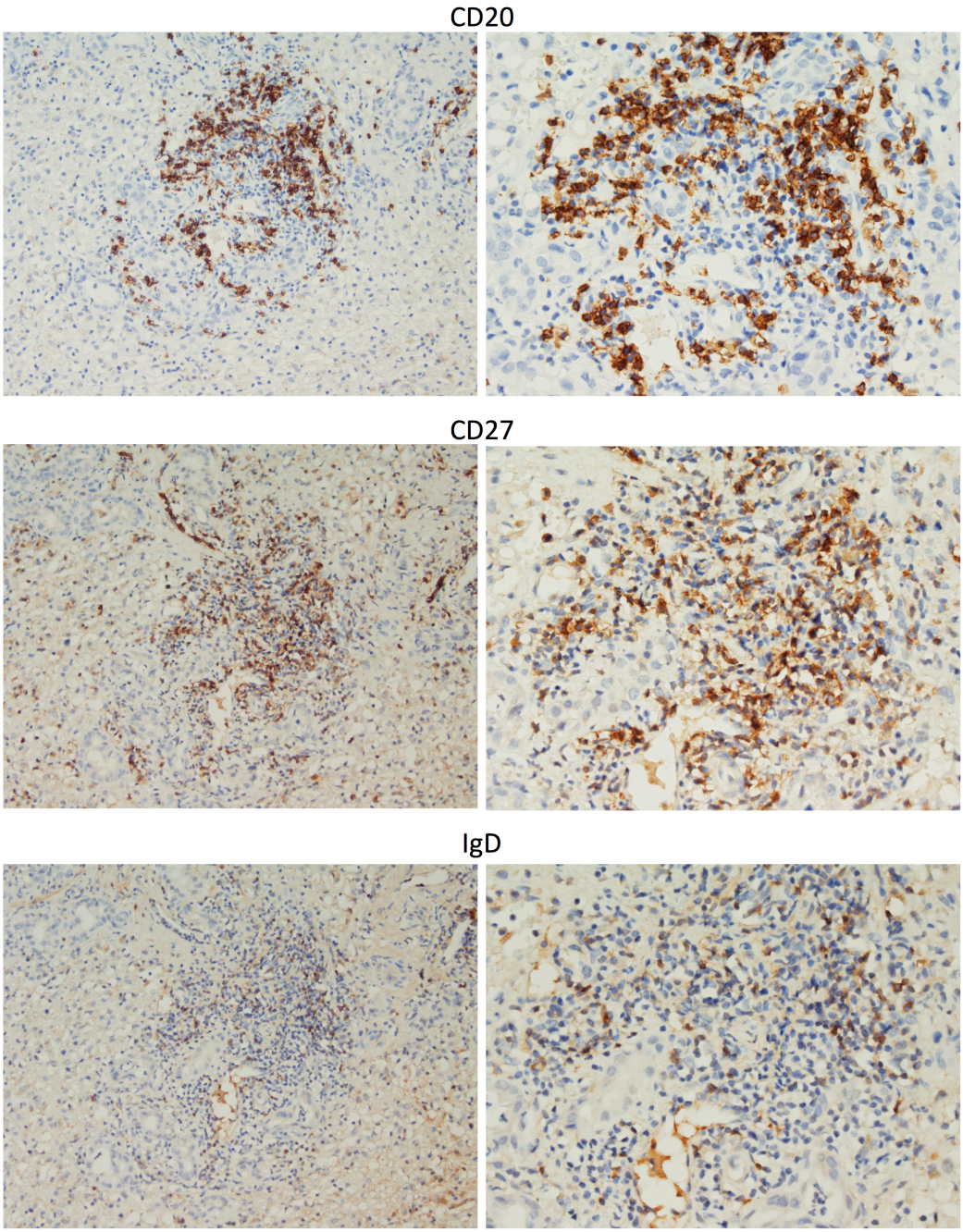


Fig. S10. Immunohistochemical staining for naïve B cells in liver tissue of a representative patient with massive hepatic necrosis at the time of liver transplantation. Liver sections were stained with monoclonal antibodies against CD 20, CD 27 and IgD. Images of liver sections at different magnification (20X and 40X). The negative staining for IgD and positive staining for CD27 indicate that the vast majority of intrahepatic B cells are not naïve.

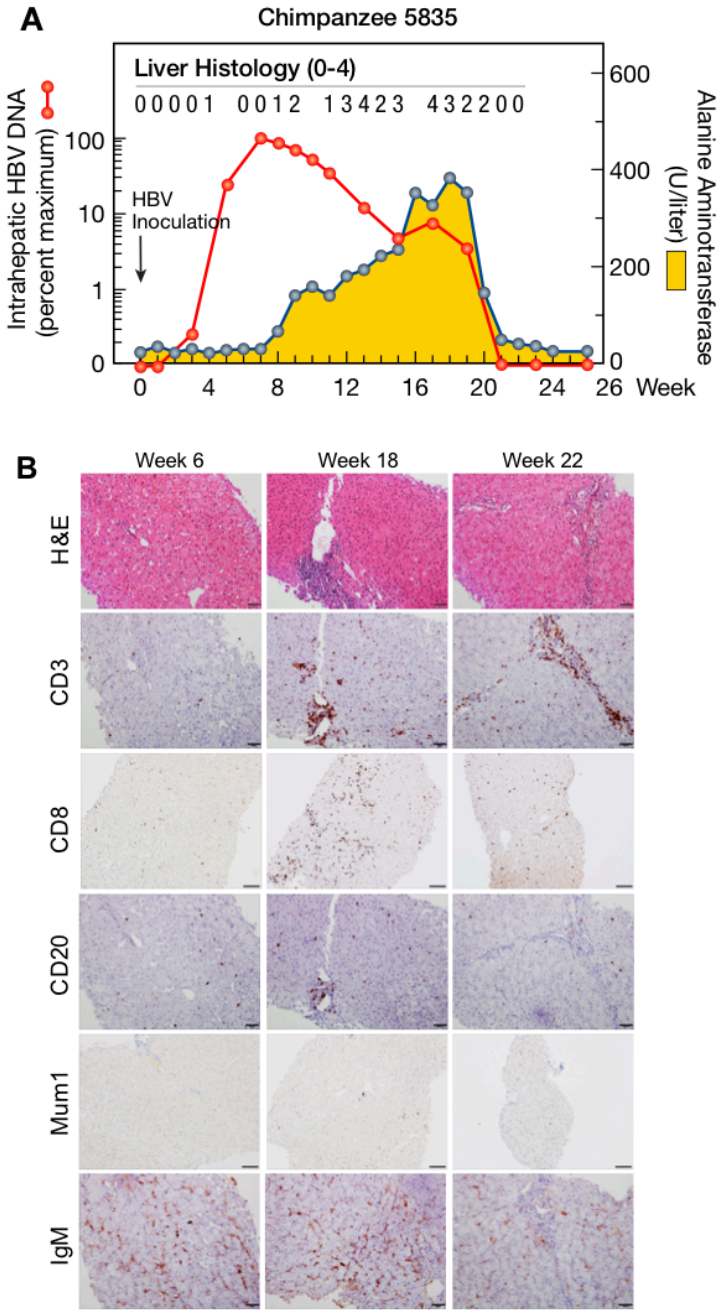


Fig. S11. Virologic and histopathologic course of acute hepatitis B in a chimpanzee infected with HBV. (A) Serum alanine aminotransferase and intrahepatic HBV DNA levels in a representative chimpanzee (no. 5835) inoculated with 108 genome equivalents of HBV strain ayw. The data on HBV DNA levels, expressed as percentage of the peak levels detected on week 6 (percent maximum), were previously reported by Wieland et al. (3). (B) immunohistochemical detection of T- and B-cell antigens in the liver of chimpanzee 5835 at three time points (week, 6, 18 and 22) during the course of acute self-limited hepatitis B. On week 18, there was extensive infiltration of CD3+CD8+ T cells, whereas CD20+ B cells, Mum+ and IgM+ plasma cells were rarely detected.

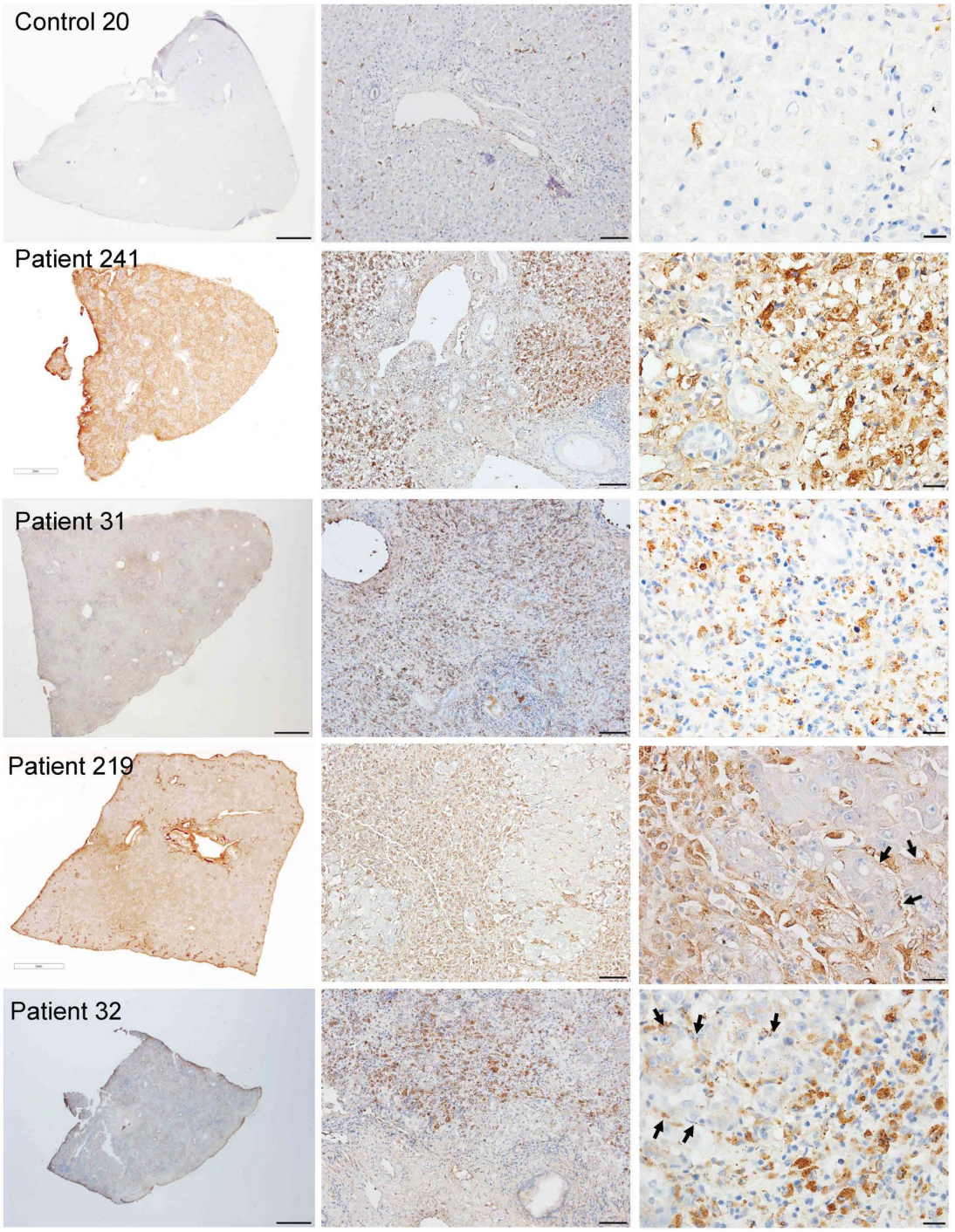


Fig. S12. Immunohistochemical staining of complement C1q in 4 patients with acute liver failure and in a representative control liver donor. Patient 241 and 31 had massive hepatic necrosis and Patient 219 and 32 had submassive hepatic necrosis. Images of liver sections at different magnification (1X, 10X and 40X, respectively, starting from the left column). Deposition of C1q is seen mainly within macrophage-like-cells, focally with a granular pattern suggestive of immune complexes, and in residual hepatocytes (arrows) showing a weak linear intercellular staining, suggesting plasma membrane deposition. Liver tissue from the control liver donor shows no significant staining for C1q.

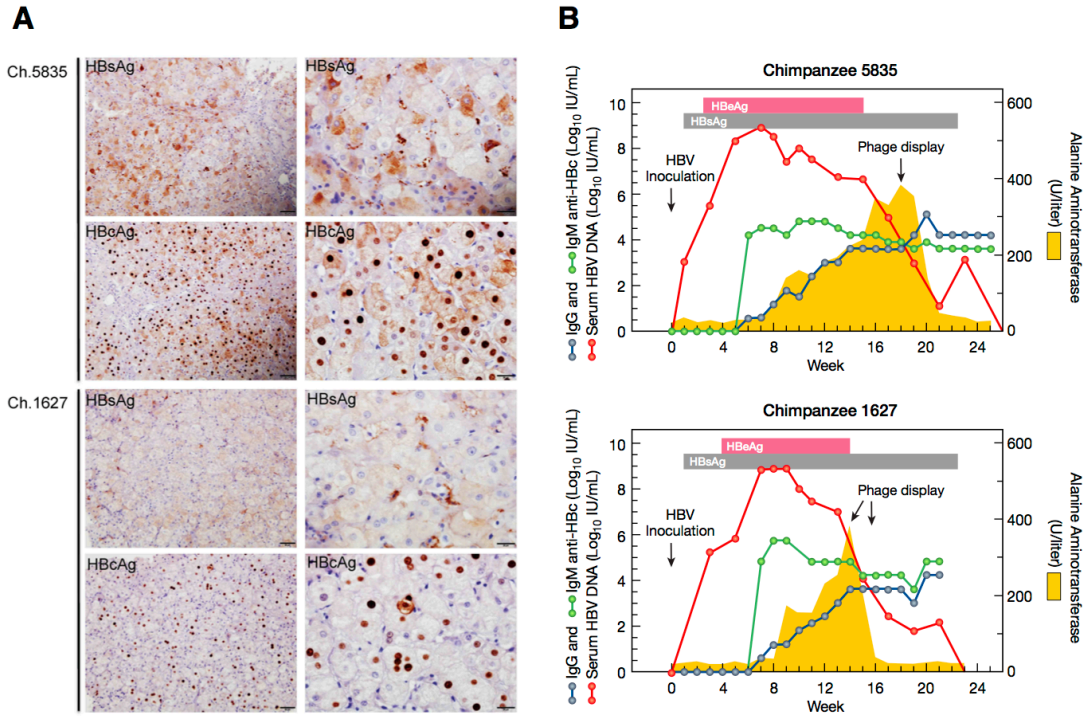


Fig. S13. Intrahepatic detection of HBsAg and HBcAg in two chimpanzees with acute, self-limited hepatitis B and timing of phage display library generation in the same chimpanzees. (A) The staining was performed at week 13 and at week 12 post-inoculation in chimpanzee 5835 and 1627, when their alanine aminotransferase values were 192U/L and 231U/L, respectively; their peak was reached at week 18 (384 U/L) and at week 14 (387U/L), respectively. HBsAg staining was diffusely positive in both chimpanzees (20X and 60X magnification). HBcAg was strongly positive in the nuclei of both animals with a diffuse cytoplasmic staining in one (chimpanzee 5835), while only one hepatocyte was positive for both nuclear and cytoplasmic staining in the second animal (chimpanzee 1627), as shown by 20X and 60X magnification. (B) The time point in which phage display libraries were generated are indicated by the arrows in relation to the clinical, serologic, and virologi course of acute HBV infection in two experimentally infected chimpanzees.

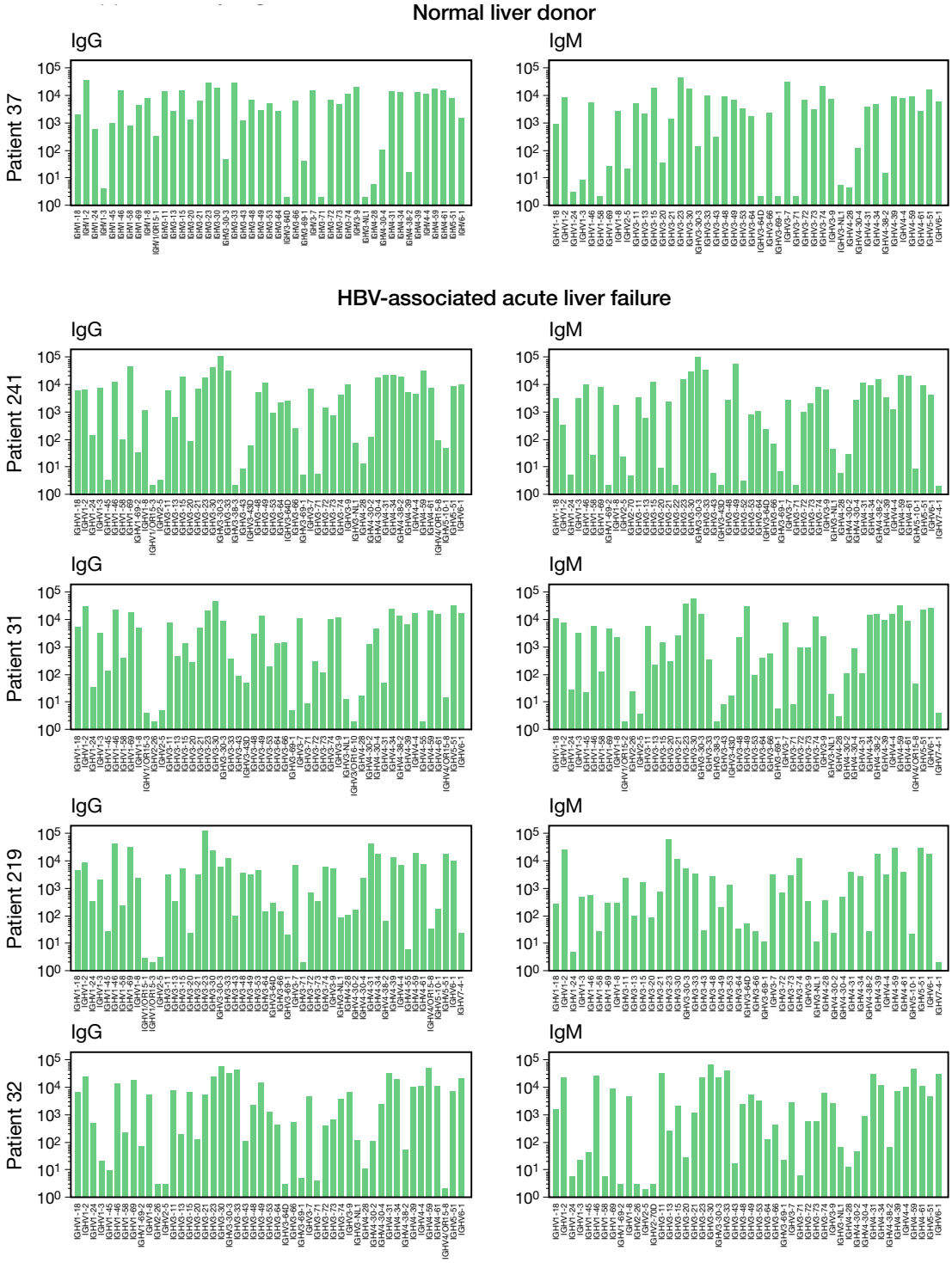


Figure S14. Distribution of IgH V gene usage in the intrahepatic IgG and IgM repertoires of a healthy liver donor (patient 37) and four HBV-associated ALF patients (241, 31, 219 and 32). Fd (IgH V region + CH1) amplicons were PCR amplified from the liver RNA with gene-specific primers, pooled, purified and characterized by next-generation sequencing (NGS). The x axis indicates the V gene segment used in each individual IgG/IgM repertoire; the y axis represents the number of unique sequences identified.

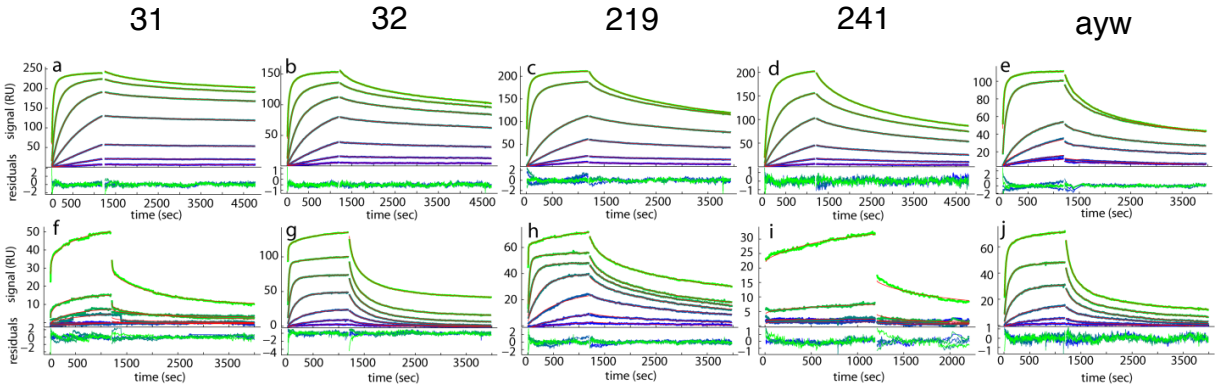


Fig. S15. Representative sensograms showing binding of monoclonal antibodies from a patient with HBV-associated acute liver failure (Fab G3: top panels) and from a chimpanzee with acute hepatitis B (Fab F8; bottom panels) to various HBcAg proteins immobilized on different sensor surfaces. Binding data (blue to green) and best-fit (red lines, superimposed by the blue/green lines) from the affinity and kinetic rate constant distribution model. For each panel, the binding traces and best-fits are shown on the top and the residuals of the fits are shown on the bottom. (A, F) HBcAg derived from patient 31; (B, G) HBcAg derived from patient 32; (C, H) HBcAg derived from patient 219; (D, I) HBcAg derived from patient 241; (E, J) HBcAg derived from wild-type ayw (8).

Table S1. Virologic features in four patients with HBV-associated acute liver failure

	Massive Hepatic Necrosis				Submassive Hepatic Necrosis			
	Patient 241		Patient 31		Patient 219		Patient 32	
Variable	**On Admission**	**Before**	**On Admission**	**Before**	**On**	**Before**	**On Admission**	**Before**
HBsAg	Positive	Negative	Positive	Positive	Positive	Negative	Borderline	Negative
Concentration (μg/mL)		0		1.74		0		0
Anti-HBs (mUI/mL)	0.6	67.7	0	0	15.3		5.9	8.0
Anti-HBc	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Titer		1:400		1:128		1:40		1:256
IgM anti-HBc	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Titer		1: 524,288		1:524,288		1: 524,288		1:524,288
HBeAg	NA	Negative	Negative	Negative	Positive		Negative	Negative
Anti-HBe	NA	Positive	Borderline	Positive	Positive		Positive	Positive
Serum HBV DNA (log_{10} IU/mL)	2.88	2.46		5.34	4.29		5.27	3.88
Liver HBV DNA (log_{10} IU/ng)		3.31		3.69		1.29		2.58
Liver HBV RNA (log_{10} IU/ng)		2.14		2.35		0.81		2.14

NA, denotes not available.

Table S2. Representative Anti-HBc IgG and IgM Titers in Four Patients with Classic Acute HBV Infection

	Anti-HBc Titers	
Acute Hepatitis B	**IgM**	**IgG**
HBV monoinfected		
Patient 1	1:41,943	1:64
Patient 2	Borderline	1:64
HBV / HCV Co-Infected		
Patient 3	1:4,096	1:128
Patient 4	1:32,768	1:8

Table S3. Demographic, clinical and pathological data of liver donors and subjects undergoing liver resection for hepatic hemangioma

Patient no.	Sex	Age	ALT	AST	GGT	Liver Pathology
Liver donors						
8	M	22	49	43	25	Mild fatty change
16	F	44	18	20	16	Very scanty fat
18	M	47	16	24	13	Mild fatty change
25	F	66	19	16	52	Mild fatty change
29	M	26	28	39	20	Normal
36	M	12	14	12	15	Normal
37	F	35	27	50	17	Normal
56	M	32	40	41	22	Normal
62	M	25	13	25	51	Mild portal inflammation
69	F	74	8	20	NA	NA
Patients undergoing liver resection						
2	F	27	26	14	27	Normal with mild sinusoidal dilatation
23	F	61	14	17	18	Normal
55	F	59	13	13	58	Normal
64	F	48	12	19	17	Normal
64	F	48	12	19	17	Normal
65	M	44	26	18	27	Normal
68	F	49	17	21	22	Very scanty fat
86	F	32	11	17	28	Normal

The demographic and clinical data of liver donor 8, 16,18, 29, 37 and 62, and all patients undergoing liver resection for hepatic hemangioma were previously published (9). NA, denotes not avaible.

Table S4. Synonymous and nonsynonymous mutations in the entire HBV genome in each of the four patients with acute liver failure

Massive hepatic necrosis: Patient 241				
Nucleotide Position*	**Change**	**Amino Acid Change**	**Region**	**Position**
1839	T to C	Ile to Thr	preC	9
1896	G to A	Trp to stop	preC	28
1899	G to A	Gly to Asp	preC	29
1909	C to T	Syn.	Core	3
1933	T to C	Syn.	Core	11
1934	A to T	Thr to Ser	Core	12
1951	G to A	Syn.	Core	17
1962	C to A	Ser to Tyr	Core	21
2003	T to A	Ser to Thr	Core	35
2009	C to T	Syn.	Core	37
2013	A to T	Tyr to Phe	Core	38
2020	A to T	Glu to Asp	Core	40
2041	T to C	Syn.	Core	47
2047	A to G	Syn.	Core	49
2080	T to C	Syn.	Core	60
2093	C to T	Syn.	Core	65
2121	T to G	Val to Gly	Core	74
2136	C to A	Pro to Gln	Core	79
2138	G to A	Ala to Thr	Core	80
2140	G to A	Ala to Thr	Core	80
2155	A to G	Syn.	Core	85
2174	A to C	Asn to His	Core	92
2198	C to A	Leu to Ile	Core	100
2226	C to T	Thr to Ile	Core	109
2227	T to A	Thr to Ile	Core	109
2287	T to C	Syn.	Core	129
2289	C to A	Pro to Gln	Core	130
2335	G to A	Syn.	Core	145
2336	A to T	Thr to Cys	Core	146
2337	C to G	Thr to Cys	Core	146
2429	C to A	Gln to Lys	Core	177
2431	A to G	Gln to Lys	Core	177
2925	C to T	Syn.	preS1	26
2934	T to C	Syn.	preS1	29
3013	T to C	Phe to Leu	preS1	56
3036	T to G	Syn.	preS1	63
3051	T to C	Syn.	preS1	68

Nucleotide Position*	Change	Amino Acid Change	Region	Position
3154	A to G	Asn to Asp	preS1	103
3159	T to C	Syn.	preS1	104
53	T to C	Phe to Leu	preS2	22
96	T to C	Leu to Pro	preS2	36
105	C to T	Ala to Val	preS2	39
148	G to A	Syn.	preS2	53
286	A to G	Syn.	S	44
346	T to C	Syn.	S	64
355	A to G	Syn.	S	67
400	C to A	Syn.	S	82
466	G to A	Syn.	S	104
499	A to C	Syn.	S	115
568	C to T	Syn.	S	138
783	G to A	Ser to Asn	S	210
784	T to C	Ser to Asn	S	210
804	C to T	Pro to Leu	S	217
813	T to A	Phe to Tyr	S	220
1613	G to A	Syn.	X	80
1634	A to T	Gln to His	X	87
1635	A to G	Ile to Val	X	88
1676	A to T	Syn.	X	101
1753	T to C	Ile to Thr	X	127
1757	G to A	Syn.	X	128
1799	C to G	Syn.	X	142
2335	G to A	Arg to Asn	P	10
2336	A to T	Arg to Asn	P	10
2337	C to G	Leu to Val	P	11
2429	C to A	Syn.	P	41
2431	A to G	Asn to Ser	P	42
2483	T to C	Syn.	P	59
2575	A to C	Lys to Thr	P	90
2609	T to C	Syn.	P	101
2645	C to A	Syn.	P	113
2708	A to G	Syn.	P	134
2925	C to T	His to Tyr	P	207
2934	T to C	Ser to Pro	P	210
3013	T to C	Phe to Ser	P	236
3036	T to G	Phe to Val	P	244
3051	T to C	Ser to Pro	P	248
3154	A to G	Lys to Arg	P	283
3159	T to C	Ser to Pro	P	285

Nucleotide Position*	Change	Amino Acid Change	Region	Position
53	T to C	Phe to Ser	P	310
96	T to C	Syn.	P	323
105	C to T	Syn.	P	326
143	G to A	Ala to Thr	P	342
286	A to G	Asn to Asp	P	388
346	T to C	Syn.	P	408
355	A to G	Asn to Asp	P	411
400	C to A	Leu to Ile	P	426
466	G to A	Ala to Thr	P	448
499	A to C	Asn to His	P	459
568	C to T	Syn.	P	482
783	G to A	Syn.	P	553
784	T to C	Ser to Pro	P	554
804	C to T	Syn.	P	560
813	T to A	Syn.	P	563
926	T to G	Ile to Arg	P	601
948	T to C	Syn.	P	608
961	A to G	Ile to Val	P	613
1050	G to T	Syn.	P	642
1053	G to A	Syn.	P	643
1060	T to C	Syn.	P	646
1068	A to C	Syn.	P	648
1293	T to C	Syn.	P	723
1613	G to A	Arg to Lys	P	830

Massive hepatic necrosis: Patient 31

Nucleotide Position*	Change	Amino Acid Change	Region	Position
1896	G to A	Trp to stop	preC	28
1934	A to T	Thr to Ser	Core	12
1962	C to A	Ser to Tyr	Core	21
1984	A to C	Syn.	Core	28
2013	A to T	Tyr to Phe	Core	38
2020	A to T	Glu to Asp	Core	40
2026	A to G	Syn.	Core	42
2045	T to A	Ser to Thr	Core	49
2063	C to A	Leu to Ile	Core	55
2075	A to G	Ile to Val	Core	59
2089	G to A	Syn.	Core	63
2092	A to G	Syn.	Core	64
2093	C to T	Syn.	Core	65

Nucleotide Position*	Change	Amino Acid Change	Region	Position
2134	T to C	Syn.	Core	78
2136	C to A	Pro to Gln	Core	79
2138	G to C	Ala to Pro	Core	80
2140	G to A	Ala to Pro	Core	80
2146	A to G	Syn.	Core	82
2237	G to C	Glu to Gln	Core	113
2246	A to T	Ile to Leu	Core	116
2288	C to G	Pro to Ala	Core	130
2291	G to C	Ala to Pro	Core	131
2304	C to A	Pro to Gln	Core	135
2336	A to T	Thr to Cys	Core	146
2337	C to G	Thr to Cys	Core	146
2345	G to A	Val to Ile	Core	149
2441	T to C	Ser to Pro	Core	181
2862	T to G	Syn.	preS1	5
2976	C to T	Syn.	preS1	43
3012	T to G	Syn.	preS1	55
3037	T to C	Syn.	preS1	64
3135	G to T	Syn.	preS1	96
3139	T to A	Ser to Thr	preS1	98
3147	T to C	Syn.	preS1	100
3148	T to G	Leu to Val	preS1	101
3153	A to G	Syn.	preS1	102
3154	A to G	Asn to Asp	preS1	103
43	A to G	Syn.	preS2	18
53	T to C	Phe to Leu	preS2	22
78	G to A	Gly to Glu	preS2	30
96	T to C	Leu to Pro	preS2	36
100	T to C	Syn.	preS2	37
111	C to A	Pro to His	preS2	41
273	A to G	Asn to Ser	S	40
288	C to A	Thr to Asn	S	45
289	T to C	Thr to Asn	S	45
346	T to C	Syn.	S	64
355	A to G	Syn.	S	67
400	C to A	Syn.	S	82
445	T to G	Syn.	S	97
499	A to C	Syn.	S	115
520	G to A	Syn.	S	122
528	T to C	Met to Thr	S	125
533	A to C	Thr to Pro	S	127

Nucleotide Position*	Change	Amino Acid Change	Region	Position
568	C to T	Syn.	S	138
783	G to A	Ser to Lys	S	210
784	T to G	Ser to Lys	S	210
791	T to A	Leu to Ile	S	213
1404	C to A	Pro to Thr	X	11
1449	T to C	Cys to Arg	X	26
1635	A to G	Ile to Val	X	88
1676	A to T	Syn.	X	101
1689	A to G	Thr to Ala	X	106
1752	A to C	Ile to Leu	X	127
1757	G to A	Syn.	X	128
2336	A to T	Arg to Ser	P	10
2337	C to G	Leu to Val	P	11
2340	G to A	Syn.	P	13
2441	T to C	Syn.	P	45
2506	T to A	Val to Glu	P	67
2534	A to G	Syn.	P	76
2549	T to C	Syn.	P	81
2553	C to T	His to Ser	P	83
2554	A to C	His to Ser	P	83
2574	A to C	Lys to Gln	P	90
2578	A to G	Lys to Arg	P	91
2591	T to C	Syn.	P	95
2636	T to C	Syn.	P	110
2645	C to T	Syn.	P	113
2662	T to G	Val to Gly	P	119
2666	C to T	Syn.	P	120
2675	A to G	Syn.	P	123
2756	T to G	Syn.	P	150
2862	T to G	Phe to Val	P	186
2976	C to T	Arg to Cys	P	224
3012	T to G	Phe to Val	P	236
3042	G to A	Val to Met	P	246
3120	A to C	Lys to Gln	P	272
3139	T to A	Val to Asp	P	278
3154	A to G	Lys to Arg	P	283
42	G to A	Syn.	P	306
43	A to G	Arg to Gly	P	307
53	T to C	Phe to Ser	P	310
78	G to A	Syn.	P	318
96	T to C	Syn.	P	324

Nucleotide Position*	Change	Amino Acid Change	Region	Position
100	T to C	Tyr to His	P	326
111	C to A	Syn.	P	329
289	T to C	Tyr to His	P	389
346	T to C	Syn.	P	408
355	A to G	Asn to Asp	P	411
400	C to A	Leu to Ile	P	426
445	T to G	Ser to Ala	P	441
499	A to C	Asn to His	P	459
520	G to C	Asp to His	P	466
533	A to C	Tyr to Ser	P	470
568	C to T	Syn.	P	482
619	C to T	Syn.	P	499
784	T to G	Ser to Ala	P	554
791	T to A	Phe to Tyr	P	556
801	T to A	Syn.	P	559
814	T to C	Syn.	P	564
842	A to C	Asn to Thr	P	573
862	T to C	Tyr to His	P	580
895	T to G	Cys to Gly	P	591
930	A to C	Gln to His	P	602
961	A to G	Ile to Val	P	613
978	T to C	Syn.	P	618
1014	T to G	Syn.	P	630
1023	C to T	Syn.	P	633
1032	A to T	Syn.	P	636
1044	T to C	Syn.	P	640
1050	G to T	Syn.	P	642
1053	G to A	Syn.	P	643
1060	T to C	Syn.	P	646
1134	C to T	Syn.	P	669
1206	C to T	Syn.	P	694
1249	T to C	Ser to Leu	P	709
1250	C to T	Ser to Leu	P	709
1272	T to C	Syn.	P	716
1323	T to C	Syn.	P	733
1350	A to C	Syn.	P	742
1404	C to A	Syn.	P	760
1449	T to C	Syn.	P	775

Submassive hepatic necrosis: Patient 219				
Nucleotide Position*	**Change**	**Amino Acid Change**	**Region**	**Position**
1828	C to A	His to Gln	preC	5
1896	G to A	Trp to stop	preC	28
1899	G to A	Gly to Asp	preC	29
1909	C to T	Syn.	Core	3
1934	A to T	Thr to Ser	Core	12
2013	A to T	Tyr to Phe	Core	38
2038	G to A	Syn.	Core	46
2041	T to C	Syn.	Core	47
2053	C to T	Syn.	Core	51
2075	A to G	Ile to Ala	Core	59
2076	T to C	Ile to Ala	Core	59
2092	A to C	Glu to Asp	Core	64
2121	T to C	Val to Ala	Core	74
2131	A to T	Glu to Asp	Core	77
2136	C to A	Pro to Gln	Core	79
2140	G to A	Syn.	Core	80
2149	C to T	Syn.	Core	83
2155	A to G	Syn.	Core	85
2158	C to T	Syn.	Core	86
2174	A to C	Asn to His	Core	92
2345	G to A	Val to Ile	Core	149
2429	C to A	Gln to Lys	Core	177
2440	A to C	Glu to Asp	Core	180
2898	C to T	Syn.	preS1	17
2918	G to A	Arg to Lys	preS1	24
2929	G to A	Ala to Thr	preS1	28
3012	T to G	Syn.	preS1	55
3090	G to A	Syn.	preS1	81
3103	A to T	Thr to Ser	preS1	86
82	A to T	Syn.	preS2	31
96	T to C	Leu to Pro	preS2	36
190	T to G	Syn.	S	12
225	G to A	Arg to Lys	S	24
286	A to G	Syn.	S	44
289	T to C	Syn.	S	45
300	T to A	Leu to His	S	49
346	T to C	Syn.	S	64
393	T to C	Phe to Ser	S	80
400	C to A	Syn.	S	82
599	A to C	Syn.	S	115

Nucleotide Position*	Change	Amino Acid Change	Region	Position
532	T to A	Syn.	S	126
592	T to C	Syn.	S	146
777	T to C	Ile to Thr	S	208
1425	T to C	Syn.	X	18
1439	C to A	Syn.	X	22
1460	C to T	Syn.	X	29
1500	T to C	Ser to Pro	X	43
1566	T to C	Ser to Pro	X	65
1635	A to T	Ile to Leu	X	88
1676	A to T	Syn.	X	101
1752	A to C	Ile to Leu	X	127
1757	G to A	Syn.	X	128
2345	G to A	Syn.	P	13
2429	C to A	Syn.	P	41
2440	A to C	Asn to Thr	P	45
2479	A to G	Asn to Ser	P	58
2556	T to C	Syn.	P	84
2573	C to T	Syn.	P	89
2576	A to C	Lys to Asn	P	90
2609	T to C	Syn.	P	101
2759	A to G	Syn.	P	151
2797	A to G	His to Arg	P	164
2840	T to G	Asp to Glu	P	178
2898	C to T	Pro to Ser	P	198
2918	G to A	Syn.	P	204
2929	G to A	Arg to His	P	208
3012	T to G	Phe to Val	P	236
3090	G to A	Ala to Thr	P	262
3103	A to T	His to Leu	P	266
82	A to T	Ser to Cys	P	320
96	T to C	Syn.	P	324
190	T to G	Ser to Ala	P	356
225	G to A	Syn.	P	367
286	A to G	Asn to Asp	P	387
289	T to C	Tyr to His	P	389
300	T to A	Syn.	P	392
346	T to C	Syn.	P	408
393	T to C	Syn.	P	423
400	C to A	Leu to Ile	P	426
499	A to C	Asn to Ile	P	459
532	T to A	Tyr to Asn	P	470

Nucleotide Position*	Change	Amino Acid Change	Region	Position
592	T to C	Syn.	P	490
777	T to C	Syn.	P	551
926	T to G	Ile to Arg	P	601
948	T to C	Syn.	P	608
987	A to G	Syn.	P	621
1050	G to T	Syn.	P	642
1053	G to A	Syn.	P	643
1060	T to C	Syn.	P	646
1068	A to C	Syn.	P	648
1250	C to T	Ser to Leu	P	709
1321	A to G	Ile to Val	P	733
1350	A to C	Syn.	P	742
1425	T to C	Syn.	P	767
1437	G to A	Syn.	P	771
1458	C to T	Syn.	P	778
1500	T to C	Syn.	P	792
1566	T to C	Syn.	P	814

Submassive hepatic necrosis: Patient 32

Nucleotide Position*	Change	Amino Acid Change	Region	Position
1896	G to A	Trp to stop	preC	28
1899	G to A	Gly to Asp	preC	29
1909	C to T	Syn.	Core	3
1980	T to C	Val to Ala	Core	27
2008	T to G	Syn.	Core	36
2060	G to A	Ala to Thr	Core	54
2121	T to C	Val to Ala	Core	74
2136	C to A	Pro to Gln	Core	79
2140	G to A	Syn.	Core	80
2164	T to C	Syn.	Core	88
2167	C to T	Syn.	Core	89
2174	A to C	Asn to His	Core	92
2203	G to A	Syn.	Core	101
2213	A to G	Ile to Val	Core	105
2242	A to C	Syn.	Core	114
2253	A to T	Tyr to Phe	Core	118
2272	G to A	Syn.	Core	124
2335	G to A	Syn.	Core	145
2339	A to T	Thr to Cys	Core	147
2340	C to G	Thr to Cys	Core	147

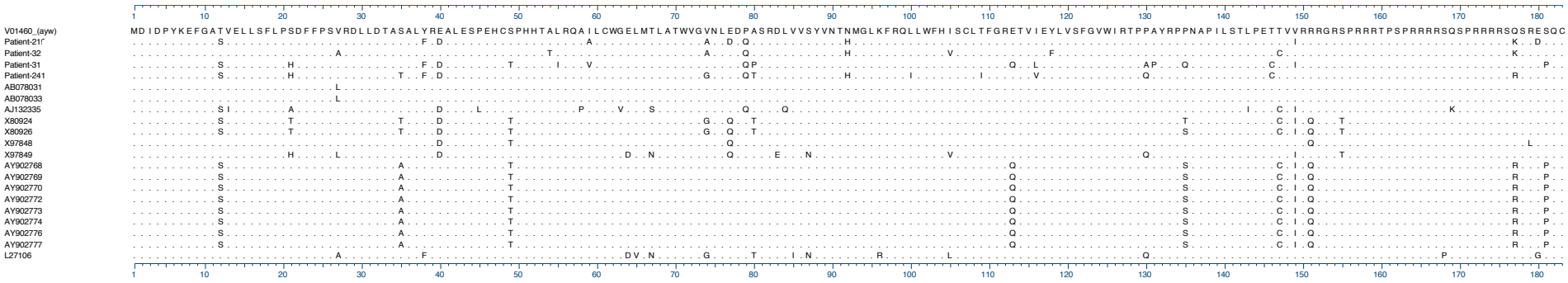
Nucleotide Position*	Change	Amino Acid Change	Region	Position
2429	C to A	Gln to Lys	Core	177
3115	T to A	Ser to Thr	preS1	90
3129	T to C	Syn.	preS1	94
80	A to G	Thr to Ala	preS2	31
96	T to C	Leu to Pro	preS2	36
176	T to C	Phe to Leu	S	8
273	A to G	Asn to Ser	S	40
289	T to C	Syn.	S	45
346	T to C	Syn.	S	64
381	G to A	Cys to Tyr	S	76
499	A to C	Syn.	S	115
562	C to A	Syn.	S	136
770	T to A	Tyr to Asn	S	206
774	G to A	Ser to Asn	S	207
1484	C to T	Syn.	X	37
1613	G to A	Syn.	X	80
1627	C to A	Ala to Asp	X	85
1633	A to G	Gln to Arg	X	87
1634	A to G	Gln to Arg	X	87
1636	T to C	Ile to Thr	X	88
1676	A to T	Syn.	X	101
1753	T to C	Ile to Thr	X	127
2335	G to A	Arg to Lys	P	10
2339	A to T	Syn.	P	11
2340	C to G	Leu to Val	P	12
2429	C to A	Syn.	P	41
2489	G to T	Syn.	P	61
2504	T to A	Syn.	P	66
2505	G to C	Val to Leu	P	67
2603	C to T	Syn.	P	99
2645	C to T	Syn.	P	113
2772	A to G	Ile to Val	P	156
2822	A to G	Syn.	P	172
3115	T to A	Val to Asp	P	270
3129	T to C	Tyr to His	P	275
80	A to G	Asn to Ser	P	319
96	T to C	Syn.	P	324
176	T to C	Ile to Thr	P	351
273	A to G	Syn.	P	383
289	T to C	Tyr to His	P	389
346	T to C	Syn.	P	408

Nucleotide Position*	Change	Amino Acid Change	Region	Position
381	G to A	Syn.	P	419
499	A to C	Asn to His	P	419
562	C to A	Leu to Met	P	480
770	T to A	Val to Glu	P	549
774	G to A	Syn.	P	550
870	A to G	Syn.	P	582
895	T to A	Cys to Ser	P	591
962	T to C	Ile to Thr	P	613
1014	T to G	Syn.	P	630
1053	G to A	Syn.	P	643
1060	T to C	Syn.	P	646
1134	C to T	Syn.	P	670
1350	A to C	Syn.	P	742
1370	T to A	Phe to Tyr	P	749
1484	C to T	Ser to Phe	P	787
1613	G to A	Arg to Lys	P	830

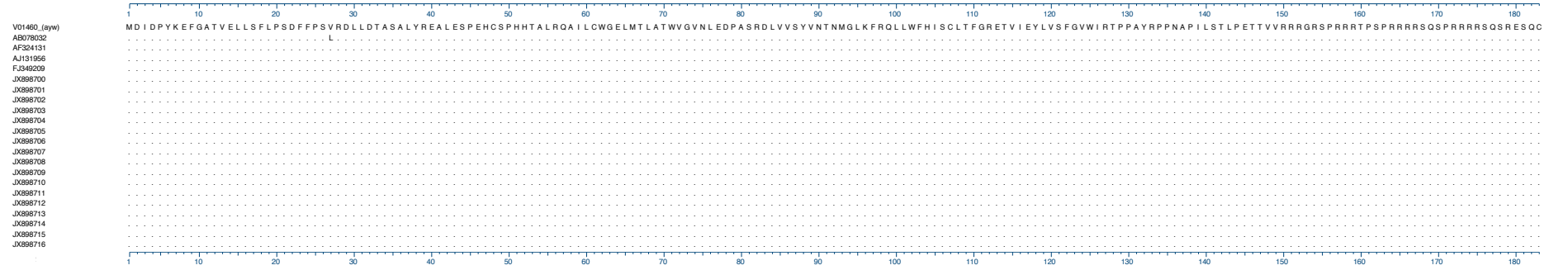
*The nucleotide position refers to to the wild- type reference HBV strain (*ayw V01460*) (8). Syn. denotes synonymous mutation; preC, pre-core; S, S region; X, X region; P, polymerase region.

Table S5. Sequence alignments of HBcAg in patients with acute liver failure and acute hepatitis B, compared to the wild-type reference HBV strain (*ayw V01460*) *(8)*

HBV-Associated Acute Liver Failure



Acute Hepatitis B



The sequence labels represent GenBank accession numbers.

Table S6. Reactivity of various anti-core antibodies against core derived from HBV wild-type (ayw) or from patients 241 and 31 with acute liver failure

Source	Antibody	Western Blots			ELISA		
		Ayw Core	241 Core	31 Core	Ayw Core	241 Core	31 Core
Commercially available	mAb (aa73-84)	-	-	-	+++	-	-
	mAb (aa1-10)	-	-	-	+++	-	-
	Rabbit polyclonal Ab	+++	-	-	+++	++	-
Patient with chronic hepatitis B	P98 serum IgG	+	+	-	++	++	++
Patients with HBV-associated acute liver failure	P32 serum IgM	++	++	-	+++	+++	++
	P241 serum IgM	-	+++	-	++	+++	++
	P219 IgM	+	+	-	+++	++	+++

Reactivity: the sign - denotes no reaction; + denotes positive reaction; ++ denotes strong reaction; +++ denotes very strong reaction.

Table S7. List of 1351 differentially expressed genes in HBV-associated acute liver failure with absolute fold change higher than 3, listed in alphabetical order

mRNA Gene Symbol	Name	Fold Change	Entrez
A1BG	alpha-1-B glycoprotein	-30.1	1
A1CF	APOBEC1 complementation factor	-6.8	29974
AADAC	arylacetamide deacetylase (esterase)	-6.3	13
AADAT	aminoadipate aminotransferase	-3.0	51166
AASS	aminoadipate-semialdehyde synthase	-4.2	10157
ABAT	4-aminobutyrate aminotransferase	-10.0	18
ABCA5	ATP-binding cassette, sub-family A (ABC1), member 5	-3.4	23461
ABCA6	ATP-binding cassette, sub-family A (ABC1), member 6	-4.6	23460
ABCA8	ATP-binding cassette, sub-family A (ABC1), member 8	-3.6	10351
ABCB4	ATP-binding cassette, sub-family B (MDR/TAP), member 4	-10.8	5244
ABCC1	ATP-binding cassette, sub-family C (CFTR/MRP), member 1	3.8	4363
ABCC2	ATP-binding cassette, sub-family C (CFTR/MRP), member 2	-4.3	1244
ABCC5	ATP-binding cassette, sub-family C (CFTR/MRP), member 5	3.5	10057
ABCC6	ATP-binding cassette, sub-family C (CFTR/MRP), member 6	-5.3	368
ABCC6P1	ATP-binding cassette, sub-family C, member 6 pseudogene 1	-6.5	653190
ABCG5	ATP-binding cassette, sub-family G (WHITE), member 5	-16.7	64240
ABCG8	ATP-binding cassette, sub-family G (WHITE), member 8	-3.5	64241
ACACB	acetyl-CoA carboxylase beta	-3.8	32
ACADL	acyl-CoA dehydrogenase, long chain	-6.7	33
ACADSB	acyl-CoA dehydrogenase, short/branched chain	-12.2	36
ACAP1	ArfGAP with coiled-coil, ankyrin repeat and PH domains 1	3.9	9744
ACAT1	acetyl-CoA acetyltransferase 1	-4.0	38
ACAT2	acetyl-CoA acetyltransferase 2	-5.6	39
ACMSD	aminocarboxymuconate semialdehyde decarboxylase	-12.8	130013
ACOT12	acyl-CoA thioesterase 12	-11.2	134526
ACOT4	acyl-CoA thioesterase 4	-3.4	122970
ACOX2	acyl-CoA oxidase 2, branched chain	-4.1	8309
ACP5	acid phosphatase 5, tartrate resistant	4.4	54
ACSL1	acyl-CoA synthetase long-chain family member 1	-4.8	2180
ACSM2A	acyl-CoA synthetase medium-chain family member 2A	-19.3	123876
ACSM3	acyl-CoA synthetase medium-chain family member 3	-4.3	6296
ACSM5	acyl-CoA synthetase medium-chain family member 5	-4.8	54988
ACSS3	acyl-CoA synthetase short-chain family member 3	-3.9	79611
ACTR3C	ARP3 actin-related protein 3 homolog C (yeast)	-5.0	653857
ADA	adenosine deaminase	4.4	100
ADAM28	ADAM metallopeptidase domain 28	3.8	10863
ADAMDEC1	ADAM-like, decysin 1	4.6	27299
ADAMTS12	ADAM metallopeptidase with thrombospondin type 1 motif, 12	5.8	81792
ADAMTS17	ADAM metallopeptidase with thrombospondin type 1 motif, 17	-4.6	170691
ADAMTS2	ADAM metallopeptidase with thrombospondin type 1 motif, 2	4.7	9509
ADAMTSL3	ADAMTS-like 3	-4.6	57188
ADAP2	ArfGAP with dual PH domains 2	3.8	55803
ADCY1	adenylate cyclase 1 (brain)	-4.7	107
ADCY7	adenylate cyclase 7	4.2	113
ADH1A	alcohol dehydrogenase 1A (class I), alpha polypeptide	-23.8	124
ADH1B	alcohol dehydrogenase 1B (class I), beta polypeptide	-6.0	125
ADH1C	alcohol dehydrogenase 1C (class I), gamma polypeptide	-15.0	126
ADH4	alcohol dehydrogenase 4 (class II), pi polypeptide	-9.8	127
ADH6	alcohol dehydrogenase 6 (class V)	-8.9	130

ADI1	acireductone dioxygenase 1	-3.0	55256
ADK	adenosine kinase	-3.5	132
ADORA3	adenosine A3 receptor	6.4	140
ADRA1A	adrenergic, alpha-1A-, receptor	-3.3	148
ADRBK2	adrenergic, beta, receptor kinase 2	3.5	157
AEBP1	AE binding protein 1	5.6	165
AFM	afamin	-11.5	173
AGBL2	ATP/GTP binding protein-like 2	-3.1	79841
AGL	amylo-alpha-1, 6-glucosidase, 4-alpha-glucanotransferase	-3.8	178
AGXT	alanine-glyoxylate aminotransferase	-14.4	189
AGXT2	alanine--glyoxylate aminotransferase 2	-15.8	64902
AGXT2L1	alanine-glyoxylate aminotransferase 2-like 1	-16.1	64850
AHSG	alpha-2-HS-glycoprotein	-12.7	197
AIF1	allograft inflammatory factor 1	4.5	199
AIM2	absent in melanoma 2	4.0	9447
AKAP13	A kinase (PRKA) anchor protein 13	3.4	11214
AKR1B1	aldo-keto reductase family 1, member B1 (aldose reductase)	6.0	231
AKR1B10	aldo-keto reductase family 1, member B10 (aldose reductase)	17.9	57016
AKR1C4	aldo-keto reductase family 1, member C4 (chlordecone reductase; 3-alpha hydroxysteroid dehydrogenase, type I; dihydrodiol dehydrogenase 4)	-7.7	1109
AKR1D1	aldo-keto reductase family 1, member D1 (delta 4-3-ketosteroid-5-beta-reductase)	-14.7	6718
ALAS1	aminolevulinate, delta-, synthase 1	-3.2	211
ALB	albumin	-11.9	213
ALDH1L1	aldehyde dehydrogenase 1 family, member L1	-4.8	10840
ALDH1L2	aldehyde dehydrogenase 1 family, member L2	3.7	160428
ALDH2	aldehyde dehydrogenase 2 family (mitochondrial)	-3.8	217
ALDH3A1	aldehyde dehydrogenase 3 family, member A1	3.9	218
ALDH4A1	aldehyde dehydrogenase 4 family, member A1	-3.6	8659
ALDH5A1	aldehyde dehydrogenase 5 family, member A1	-5.2	7915
ALDH6A1	aldehyde dehydrogenase 6 family, member A1	-9.4	4329
ALDH8A1	aldehyde dehydrogenase 8 family, member A1	-14.7	64577
ALDOA	aldolase A, fructose-bisphosphate	3.1	226
ALDOB	aldolase B, fructose-bisphosphate	-6.5	229
ALOX5	arachidonate 5-lipoxygenase	4.4	240
ALS2	amyotrophic lateral sclerosis 2 (juvenile)	-4.3	57679
AMBP	alpha-1-microglobulin/bikunin precursor	-3.9	259
AMDHD1	amidohydrolase domain containing 1	-46.7	144193
AMICA1	adhesion molecule, interacts with CXADR antigen 1	3.7	120425
ANG	angiogenin, ribonuclease, RNase A family, 5	-6.4	283
ANGPTL3	angiopoietin-like 3	-12.2	27329
ANK3	ankyrin 3, node of Ranvier (ankyrin G)	3.0	288
ANKRD36	ankyrin repeat domain 36	5.0	375248
ANKRD36B	ankyrin repeat domain 36B	4.3	57730
ANKRD36BP2	ankyrin repeat domain 36B pseudogene 2	12.1	645784
ANLN	anillin, actin binding protein	5.4	54443
ANO3	anoctamin 3	3.9	63982
ANTXR1	anthrax toxin receptor 1	4.3	84168
ANXA1	annexin A1	4.0	301
ANXA10	annexin A10	-17.0	11199
ANXA13	annexin A13	5.0	312
ANXA2	annexin A2	3.9	302
ANXA2P2	annexin A2 pseudogene 2	3.4	304
ANXA3	annexin A3	5.2	306
AOAH	acyloxyacyl hydrolase (neutrophil)	4.2	313

AOX1	aldehyde oxidase 1	-25.0	316
APOA1	apolipoprotein A-I	-11.3	335
APOA2	apolipoprotein A-II	-5.9	336
APOA5	apolipoprotein A-V	-5.3	116519
APOB	apolipoprotein B (including Ag(x) antigen)	-5.2	338
APOBEC3B	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3B	6.4	9582
APOBEC3G	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3G	7.3	60489
APOC2	apolipoprotein C-II	-3.5	344
APOC3	apolipoprotein C-III	-5.9	345
APOC4	apolipoprotein C-IV	-4.9	346
APOF	apolipoprotein F	-51.3	319
APOH	apolipoprotein H (beta-2-glycoprotein I)	-8.9	350
APOM	apolipoprotein M	-7.8	55937
APOOL	apolipoprotein O-like	-3.1	139322
AQP1	aquaporin 1 (Colton blood group)	3.5	358
AQP11	aquaporin 11	-3.0	282679
AQP3	aquaporin 3 (Gill blood group)	-3.1	360
AQP9	aquaporin 9	-8.2	366
AR	androgen receptor	-5.4	367
AREG	amphiregulin	5.4	374
ARG1	arginase, liver	-17.9	383
ARHGAP15	Rho GTPase activating protein 15	3.5	55843
ARHGAP25	Rho GTPase activating protein 25	3.6	9938
ARHGAP30	Rho GTPase activating protein 30	4.6	257106
ARHGAP9	Rho GTPase activating protein 9	4.5	64333
ARHGDIB	Rho GDP dissociation inhibitor (GDI) beta	4.5	397
ARHGEF26	Rho guanine nucleotide exchange factor (GEF) 26	-4.3	26084
ARHGEF3	Rho guanine nucleotide exchange factor (GEF) 3	3.5	50650
ARHGEF6	Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6	3.0	9459
ARL4C	ADP-ribosylation factor-like 4C	6.0	10123
ARSE	arylsulfatase E (chondrodysplasia punctata 1)	-3.7	415
AS3MT	arsenic (+3 oxidation state) methyltransferase	-4.6	57412
ASGR1	asialoglycoprotein receptor 1	-7.8	432
ASGR2	asialoglycoprotein receptor 2	-5.7	433
ASL	argininosuccinate lyase	-4.5	435
ASPHD2	aspartate beta-hydroxylase domain containing 2	5.1	57168
ASS1	argininosuccinate synthase 1	-5.0	445
ATF5	activating transcription factor 5	-8.3	22809
ATG2B	ATG2 autophagy related 2 homolog B (S. cerevisiae)	-3.5	55102
ATP2B2	ATPase, Ca++ transporting, plasma membrane 2	-6.4	491
ATP7B	ATPase, Cu++ transporting, beta polypeptide	-5.4	540
AVPR1A	arginine vasopressin receptor 1A	-4.0	552
AZGP1	alpha-2-glycoprotein 1, zinc-binding	-23.1	563
B7H6	B7 homolog 6	3.1	374383
BAAT	bile acid CoA: amino acid N-acyltransferase (glycine N-choloyltransferase)	-4.1	570
BACE2	beta-site APP-cleaving enzyme 2	3.8	25825
BASP1	brain abundant, membrane attached signal protein 1	5.1	10409
BBOX1	butyrobetaine (gamma), 2-oxoglutarate dioxygenase (gamma-butyrobetaine hydroxylase) 1	-3.7	8424
BCAT1	branched chain amino-acid transaminase 1, cytosolic	5.5	586
BCHE	butyrylcholinesterase	-8.1	590
BCKDHB	branched chain keto acid dehydrogenase E1, beta polypeptide	-4.1	594
BCL11B	B-cell CLL/lymphoma 11B (zinc finger protein)	4.2	64919

BCL2	B-cell CLL/lymphoma 2	3.4	596
BCO2	beta-carotene oxygenase 2	-4.9	83875
BDH1	3-hydroxybutyrate dehydrogenase, type 1	-5.4	622
BEX4	brain expressed, X-linked 4	4.1	56271
BGN	biglycan	4.3	633
BHLHE41	basic helix-loop-helix family, member e41	4.9	79365
BHMT	betaine--homocysteine S-methyltransferase	-4.5	635
BHMT2	betaine--homocysteine S-methyltransferase 2	-10.5	23743
BICC1	bicaudal C homolog 1 (Drosophila)	4.1	80114
BLNK	B-cell linker	-3.0	29760
BNIP3	BCL2/adenovirus E1B 19kDa interacting protein 3	-3.3	664
BRP44	brain protein 44	-3.6	25874
BUB1	budding uninhibited by benzimidazoles 1 homolog (yeast)	4.0	699
BUB1B	budding uninhibited by benzimidazoles 1 homolog beta (yeast)	5.2	701
C10orf128	chromosome 10 open reading frame 128	3.0	170371
C10orf54	chromosome 10 open reading frame 54	3.6	64115
C10orf57	chromosome 10 open reading frame 57	-3.5	80195
C11orf80	chromosome 11 open reading frame 80	3.1	79703
C12orf75	chromosome 12 open reading frame 75	7.2	387882
C14orf28	chromosome 14 open reading frame 28	-4.2	122525
C15orf52	chromosome 15 open reading frame 52	3.2	388115
C16orf54	chromosome 16 open reading frame 54	6.6	283897
C18orf18	chromosome 18 open reading frame 18	-3.3	147525
C1orf106	chromosome 1 open reading frame 106	4.7	55765
C1orf115	chromosome 1 open reading frame 115	-5.0	79762
C1orf116	chromosome 1 open reading frame 116	3.6	79098
C1orf162	chromosome 1 open reading frame 162	8.2	128346
C1orf168	chromosome 1 open reading frame 168	-4.5	199920
C1orf226	chromosome 1 open reading frame 226	-3.5	400793
C1orf38	chromosome 1 open reading frame 38	5.9	9473
C1orf53	chromosome 1 open reading frame 53	-3.2	388722
C1orf54	chromosome 1 open reading frame 54	5.0	79630
C1QA	complement component 1, q subcomponent, A chain	10.1	712
C1QB	complement component 1, q subcomponent, B chain	12.9	713
C1QC	complement component 1, q subcomponent, C chain	6.5	714
C1R	complement component 1, r subcomponent	-3.2	715
C1RL	complement component 1, r subcomponent-like	-4.4	51279
C1S	complement component 1, s subcomponent	-6.1	716
C2	complement component 2	-4.0	717
C20orf3	chromosome 20 open reading frame 3	-3.5	57136
C2orf72	chromosome 2 open reading frame 72	-3.1	257407
C3AR1	complement component 3a receptor 1	3.1	719
C3orf23	chromosome 3 open reading frame 23	-3.1	285343
C3orf52	chromosome 3 open reading frame 52	3.0	79669
C3P1	complement component 3 precursor pseudogene	-18.7	388503
C4BPA	complement component 4 binding protein, alpha	-18.4	722
C4BPB	complement component 4 binding protein, beta	-20.5	725
C4orf19	chromosome 4 open reading frame 19	-3.9	55286
C4orf34	chromosome 4 open reading frame 34	-4.3	201895
C4orf48	chromosome 4 open reading frame 48	5.6	401115
C5	complement component 5	-15.3	727
C5AR1	complement component 5a receptor 1	3.4	728
C5orf27	chromosome 5 open reading frame 27	-6.1	202299
C6	complement component 6	-10.4	729
C6orf145	chromosome 6 open reading frame 145	-3.3	221749
C8A	complement component 8, alpha polypeptide	-39.1	731

C8B	complement component 8, beta polypeptide	-35.7	732
C8G	complement component 8, gamma polypeptide	-6.2	733
C8orf38	chromosome 8 open reading frame 38	-3.1	137682
C8orf46	chromosome 8 open reading frame 46	-6.5	254778
C9	complement component 9	-117.7	735
C9orf16	chromosome 9 open reading frame 16	3.5	79095
CA12	carbonic anhydrase XII	3.3	771
CA2	carbonic anhydrase II	-7.4	760
CA5A	carbonic anhydrase VA, mitochondrial	-4.2	763
CAPG	capping protein (actin filament), gelsolin-like	5.4	822
CAPN5	calpain 5	-3.0	726
CAPN6	calpain 6	3.7	827
CARD16	caspase recruitment domain family, member 16	4.8	114769
CBLB	Cas-Br-M (murine) ecotropic retroviral transforming sequence b	3.1	868
CBS	cystathionine-beta-synthase	-5.2	875
CCDC102B	coiled-coil domain containing 102B	6.5	79839
CCDC109B	coiled-coil domain containing 109B	3.8	55013
CCDC146	coiled-coil domain containing 146	4.8	57639
CCDC80	coiled-coil domain containing 80	4.2	151887
CCDC88A	coiled-coil domain containing 88A	3.6	55704
CCL16	chemokine (C-C motif) ligand 16	-5.7	6360
CCL18	chemokine (C-C motif) ligand 18 (pulmonary and activation-regulated)	8.0	6362
CCL5	chemokine (C-C motif) ligand 5	9.2	6352
CCNB1	cyclin B1	5.1	891
CCNB2	cyclin B2	3.7	9133
CCND2	cyclin D2	4.0	894
CCR1	chemokine (C-C motif) receptor 1	3.4	1230
CCR2	chemokine (C-C motif) receptor 2	8.0	729230
CCR5	chemokine (C-C motif) receptor 5	4.7	1234
CCR7	chemokine (C-C motif) receptor 7	3.5	1236
CCRL2	chemokine (C-C motif) receptor-like 2	3.6	9034
CD163	CD163 molecule	5.0	9332
CD163	CD163 molecule	4.6	9332
CD2	CD2 molecule	8.5	914
CD209	CD209 molecule	3.2	30835
CD24	CD24 molecule	4.2	1E+08
CD27	CD27 molecule	4.9	939
CD300A	CD300a molecule	4.1	11314
CD300LF	CD300 molecule-like family member f	4.5	146722
CD302	CD302 molecule	-5.3	9936
CD38	CD38 molecule	3.1	952
CD3D	CD3d molecule, delta (CD3-TCR complex)	5.3	915
CD3G	CD3g molecule, gamma (CD3-TCR complex)	4.6	917
CD44	CD44 molecule (Indian blood group)	3.2	960
CD52	CD52 molecule	11.7	1043
CD53	CD53 molecule	4.5	963
CD72	CD72 molecule	4.9	971
CD74	CD74 molecule, major histocompatibility complex, class II invariant chain	6.5	972
CD84	CD84 molecule	4.8	8832
CD86	CD86 molecule	5.2	942
CD8A	CD8a molecule	6.6	925
CD8B	CD8b molecule	4.0	926
CD93	CD93 molecule	3.7	22918
CD97	CD97 molecule	4.1	976

CDC14B	CDC14 cell division cycle 14 homolog B (S. cerevisiae)	-3.4	8555
CDC20	cell division cycle 20 homolog (S. cerevisiae)	5.8	991
CDC37L1	cell division cycle 37 homolog (S. cerevisiae)-like 1	-3.1	55664
CDC42EP5	CDC42 effector protein (Rho GTPase binding) 5	4.1	148170
CDCP1	CUB domain containing protein 1	3.3	64866
CDH11	cadherin 11, type 2, OB-cadherin (osteoblast)	3.1	1009
CDH6	cadherin 6, type 2, K-cadherin (fetal kidney)	3.2	1004
CDO1	cysteine dioxygenase, type I	-31.4	1036
CEBPA	CCAAT/enhancer binding protein (C/EBP), alpha	-3.1	1050
CEBPD	CCAAT/enhancer binding protein (C/EBP), delta	-3.4	1052
CECR1	cat eye syndrome chromosome region, candidate 1	8.4	51816
CELF2	CUGBP, Elav-like family member 2	4.1	10659
CENPF	centromere protein F, 350/400kDa (mitosin)	3.3	1063
CENPV	centromere protein V	-3.3	201161
CEP128	centrosomal protein 128kDa	4.2	145508
CEP55	centrosomal protein 55kDa	3.4	55165
CERS2	ceramide synthase 2	-4.0	29956
CES1	carboxylesterase 1	-9.1	1066
CES2	carboxylesterase 2	-3.3	8824
CFB	complement factor B	-5.9	629
CFD	complement factor D (adipsin)	8.9	1675
CFH	complement factor H	-5.3	3075
CFHR2	complement factor H-related 2	-13.3	3080
CFHR3	complement factor H-related 3	-54.0	10878
CFHR4	complement factor H-related 4	-73.1	10877
CFHR5	complement factor H-related 5	-50.8	81494
CFI	complement factor I	-7.3	3426
CFL2	cofilin 2 (muscle)	-4.1	1073
CFP	complement factor properdin	8.0	5199
CFTR	cystic fibrosis transmembrane conductance regulator (ATP-binding cassette sub-family C, member 7)	3.3	1080
CGNL1	cingulin-like 1	-4.0	84952
CHN2	chimerin (chimaerin) 2	-3.6	1124
CHPT1	choline phosphotransferase 1	-3.3	56994
CHST11	carbohydrate (chondroitin 4) sulfotransferase 11	3.9	50515
CHST2	carbohydrate (N-acetylglucosamine-6-O) sulfotransferase 2	3.4	9435
CHST4	carbohydrate (N-acetylglucosamine 6-O) sulfotransferase 4	3.5	10164
CIDEB	cell death-inducing DFFA-like effector b	-3.0	27141
CIITA	class II, major histocompatibility complex, transactivator	3.4	4261
CKAP2	cytoskeleton associated protein 2	9.8	26586
CLDN10	claudin 10	3.8	9071
CLDN11	claudin 11	6.3	5010
CLDN12	claudin 12	-3.2	9069
CLEC11A	C-type lectin domain family 11, member A	3.6	6320
CLEC12A	C-type lectin domain family 12, member A	3.6	160364
CLEC7A	C-type lectin domain family 7, member A	3.3	64581
CLIC2	chloride intracellular channel 2	3.3	1193
CLIC6	chloride intracellular channel 6	6.3	54102
CLIP4	CAP-GLY domain containing linker protein family, member 4	3.0	79745
CLRN3	clarin 3	-8.1	119467
CLU	clusterin	-5.9	1191
CMKLR1	chemokine-like receptor 1	5.5	1240
CMTM7	CKLF-like MARVEL transmembrane domain containing 7	5.2	112616
CMTM8	CKLF-like MARVEL transmembrane domain containing 8	-4.1	152189
CNDP1	carnosine dipeptidase 1 (metallopeptidase M20 family)	-13.8	84735
CNGA1	cyclic nucleotide gated channel alpha 1	-3.1	1259

CNTLN	centlein, centrosomal protein	-3.8	54875
CNTN3	contactin 3 (plasmacytoma associated)	-3.2	5067
COBLL1	COBL-like 1	-3.8	22837
COL16A1	collagen, type XVI, alpha 1	3.4	1307
COL1A1	collagen, type I, alpha 1	9.0	1277
COL1A2	collagen, type I, alpha 2	8.3	1278
COL3A1	collagen, type III, alpha 1	5.2	1281
COL4A1	collagen, type IV, alpha 1	5.6	1282
COL4A2	collagen, type IV, alpha 2	6.8	1284
COL4A4	collagen, type IV, alpha 4	3.8	1286
COL5A1	collagen, type V, alpha 1	6.3	1289
COL5A2	collagen, type V, alpha 2	3.5	1290
COL6A1	collagen, type VI, alpha 1	3.1	1291
COL6A2	collagen, type VI, alpha 2	3.8	1292
COL6A3	collagen, type VI, alpha 3	4.6	1293
CORO1A	coronin, actin binding protein, 1A	5.7	11151
COTL1	coactosin-like 1 (Dictyostelium)	5.1	23406
CP	ceruloplasmin (ferroxidase)	-17.8	1356
CPEB3	cytoplasmic polyadenylation element binding protein 3	-3.9	22849
CPN1	carboxypeptidase N, polypeptide 1	-26.2	1369
CPN2	carboxypeptidase N, polypeptide 2	-7.3	1370
CPS1	carbamoyl-phosphate synthase 1, mitochondrial	-8.9	1373
CPVL	carboxypeptidase, vitellogenic-like	5.9	54504
CR1	complement component (3b/4b) receptor 1 (Knops blood group)	4.5	1378
CREB5	cAMP responsive element binding protein 5	4.0	9586
CRIM1	cysteine rich transmembrane BMP regulator 1 (chordin-like)	3.1	51232
CRIP1	cysteine-rich protein 1 (intestinal)	4.4	1396
CROT	carnitine O-octanoyltransferase	-3.1	54677
CRYAB	crystallin, alpha B	3.7	1410
CRYZ	crystallin, zeta (quinone reductase)	-3.2	1429
CSAD	cysteine sulfinic acid decarboxylase	-3.0	51380
CSF1R	colony stimulating factor 1 receptor	5.4	1436
CST7	cystatin F (leukocystatin)	4.1	8530
CTBS	chitobiase, di-N-acetyl-	-3.3	1486
CTH	cystathionase (cystathionine gamma-lyase)	-8.7	1491
CTHRC1	collagen triple helix repeat containing 1	14.1	115908
CTLA4	cytotoxic T-lymphocyte-associated protein 4	4.6	1493
CTSC	cathepsin C	4.9	1075
CTSE	cathepsin E	6.2	1510
CTSS	cathepsin S	4.0	1520
CUX2	cut-like homeobox 2	-6.8	23316
CXCL14	chemokine (C-X-C motif) ligand 14	5.2	9547
CXCL2	chemokine (C-X-C motif) ligand 2	-4.2	2920
CXCL5	chemokine (C-X-C motif) ligand 5	8.9	6374
CXCL6	chemokine (C-X-C motif) ligand 6 (granulocyte chemotactic protein 2)	6.7	6372
CXCR4	chemokine (C-X-C motif) receptor 4	5.3	7852
CXCR6	chemokine (C-X-C motif) receptor 6	5.3	10663
CYB5A	cytochrome b5 type A (microsomal)	-4.4	1528
CYBA	cytochrome b-245, alpha polypeptide	7.9	1535
CYBB	cytochrome b-245, beta polypeptide	3.0	1536
CYP1A1	cytochrome P450, family 1, subfamily A, polypeptide 1	-7.2	1543
CYP1A2	cytochrome P450, family 1, subfamily A, polypeptide 2	-13.7	1544
CYP26A1	cytochrome P450, family 26, subfamily A, polypeptide 1	-5.3	1592
CYP26B1	cytochrome P450, family 26, subfamily B, polypeptide 1	3.6	56603
CYP27A1	cytochrome P450, family 27, subfamily A, polypeptide 1	-3.8	1593

CYP2B6	cytochrome P450, family 2, subfamily B, polypeptide 6	-10.5	1555
CYP2C18	cytochrome P450, family 2, subfamily C, polypeptide 18	-7.2	1562
CYP2C19	cytochrome P450, family 2, subfamily C, polypeptide 19	-6.9	1557
CYP2C8	cytochrome P450, family 2, subfamily C, polypeptide 8	-12.4	1558
CYP2C9	cytochrome P450, family 2, subfamily C, polypeptide 9	-8.4	1559
CYP2D6	cytochrome P450, family 2, subfamily D, polypeptide 6	-8.2	1565
CYP2E1	cytochrome P450, family 2, subfamily E, polypeptide 1	-13.6	1571
CYP2J2	cytochrome P450, family 2, subfamily J, polypeptide 2	-6.2	1573
CYP39A1	cytochrome P450, family 39, subfamily A, polypeptide 1	-6.8	51302
CYP3A4	cytochrome P450, family 3, subfamily A, polypeptide 4	-6.9	1576
CYP3A43	cytochrome P450, family 3, subfamily A, polypeptide 43	-3.9	64816
CYP3A5	cytochrome P450, family 3, subfamily A, polypeptide 5	-5.4	1577
CYP3A7	cytochrome P450, family 3, subfamily A, polypeptide 7	-5.7	1551
CYP4A11	cytochrome P450, family 4, subfamily A, polypeptide 11	-7.5	1579
CYP4F2	cytochrome P450, family 4, subfamily F, polypeptide 2	-17.8	8529
CYP4F3	cytochrome P450, family 4, subfamily F, polypeptide 3	-27.9	4051
CYP4V2	cytochrome P450, family 4, subfamily V, polypeptide 2	-3.2	285440
CYP51A1	cytochrome P450, family 51, subfamily A, polypeptide 1	-3.4	1595
CYP8B1	cytochrome P450, family 8, subfamily B, polypeptide 1	-19.0	1582
CYSLTR1	cysteinyl leukotriene receptor 1	3.7	10800
CYTIP	cytohesin 1 interacting protein	7.3	9595
DBN1	drebrin 1	3.7	1627
DCDC2	doublecortin domain containing 2	3.9	51473
DCXR	dicarbonyl/L-xylulose reductase	-3.6	51181
DDC	dopa decarboxylase (aromatic L-amino acid decarboxylase)	-4.4	1644
DECR2	2,4-dienoyl CoA reductase 2, peroxisomal	-3.6	26063
DEF6	differentially expressed in FDCP 6 homolog (mouse)	3.9	50619
DEPDC7	DEP domain containing 7	-11.4	91614
DERL3	Der1-like domain family, member 3	3.0	91319
DGAT2	diacylglycerol O-acyltransferase 2	-4.5	84649
DHCR24	24-dehydrocholesterol reductase	-4.6	1718
DHCR7	7-dehydrocholesterol reductase	-3.8	1717
DHODH	dihydroorotate dehydrogenase (quinone)	-10.3	1723
DIO1	deiodinase, iodothyronine, type I	-18.0	1733
DLGAP5	discs, large (Drosophila) homolog-associated protein 5	5.9	9787
DMGDH	dimethylglycine dehydrogenase	-16.7	29958
DNAJB9	DnaJ (Hsp40) homolog, subfamily B, member 9	-3.9	4189
DNAJC12	DnaJ (Hsp40) homolog, subfamily C, member 12	-5.8	56521
DOCK10	dedicator of cytokinesis 10	3.5	55619
DOCK11	dedicator of cytokinesis 11	3.8	139818
DOCK2	dedicator of cytokinesis 2	5.9	1794
DOCK8	dedicator of cytokinesis 8	4.0	81704
DOK3	docking protein 3	5.7	79930
DPEP2	dipeptidase 2	7.9	64174
DPYS	dihydropyrimidinase	-12.3	1807
DSC2	desmocollin 2	3.3	1824
DTNA	dystrobrevin, alpha	3.6	1837
DUSP10	dual specificity phosphatase 10	-3.4	11221
DUSP4	dual specificity phosphatase 4	3.5	1846
EBP	emopamil binding protein (sterol isomerase)	-4.3	10682
ECHDC2	enoyl CoA hydratase domain containing 2	-3.2	55268
ECI2	enoyl-CoA delta isomerase 2	-3.0	10455
EDN1	endothelin 1	3.1	1906
EFEMP1	EGF containing fibulin-like extracellular matrix protein 1	4.1	2202
EFEMP2	EGF containing fibulin-like extracellular matrix protein 2	3.2	30008
EFNA1	ephrin-A1	-4.9	1942

EHF	ets homologous factor	4.0	26298
EHHADH	enoyl-CoA, hydratase/3-hydroxyacyl CoA dehydrogenase	-6.5	1962
ELF4	E74-like factor 4 (ets domain transcription factor)	4.5	2000
ELOVL2	ELOVL fatty acid elongase 2	-5.9	54898
ELOVL6	ELOVL fatty acid elongase 6	-4.1	79071
ELOVL7	ELOVL fatty acid elongase 7	5.9	79993
EMILIN1	elastin microfibril interfacer 1	3.2	11117
EMILIN2	elastin microfibril interfacer 2	4.6	84034
EMP3	epithelial membrane protein 3	5.0	2014
ENPEP	glutamyl aminopeptidase (aminopeptidase A)	-3.9	2028
ENPP1	ectonucleotide pyrophosphatase/phosphodiesterase 1	-6.2	5167
ENTPD1	ectonucleoside triphosphate diphosphohydrolase 1	3.1	953
EOMES	eomesodermin	3.1	8320
EPB41L3	erythrocyte membrane protein band 4.1-like 3	3.8	23136
EPB41L4B	erythrocyte membrane protein band 4.1 like 4B	-3.9	54566
EPB41L5	erythrocyte membrane protein band 4.1 like 5	-5.9	57669
EPCAM	epithelial cell adhesion molecule	10.3	4072
EPHX2	epoxide hydrolase 2, cytoplasmic	-6.2	2053
EPT1	ethanolaminephosphotransferase 1 (CDP-ethanolamine-specific)	-4.1	85465
ERBB3	v-erb-b2 erythroblastic leukemia viral oncogene homolog 3 (avian)	-3.1	2065
ERLIN1	ER lipid raft associated 1	-3.4	10613
ERRFI1	ERBB receptor feedback inhibitor 1	-3.3	54206
ESR1	estrogen receptor 1	-3.7	2099
ESRP2	epithelial splicing regulatory protein 2	-4.3	80004
ETFDH	electron-transferring-flavoprotein dehydrogenase	-4.6	2110
ETNK2	ethanolamine kinase 2	-3.1	55224
ETS2	v-ets erythroblastosis virus E26 oncogene homolog 2 (avian)	-3.7	2114
EVI2A	ecotropic viral integration site 2A	5.7	2123
EVI2B	ecotropic viral integration site 2B	4.6	2124
EXPH5	exophilin 5	-4.1	23086
F10	coagulation factor X	-4.5	2159
F11	coagulation factor XI	-3.1	2160
F12	coagulation factor XII (Hageman factor)	-12.9	2161
F13B	coagulation factor XIII, B polypeptide	-14.2	2165
F2	coagulation factor II (thrombin)	-22.7	2147
F5	coagulation factor V (proaccelerin, labile factor)	-5.8	2153
F7	coagulation factor VII (serum prothrombin conversion accelerator)	-3.1	2155
F9	coagulation factor IX	-69.1	2158
FABP1	fatty acid binding protein 1, liver	-6.8	2168
FABP3	fatty acid binding protein 3, muscle and heart (mammary-derived growth inhibitor)	5.6	2170
FABP4	fatty acid binding protein 4, adipocyte	5.3	2167
FABP5	fatty acid binding protein 5 (psoriasis-associated)	7.0	2171
FAM110C	family with sequence similarity 110, member C	-4.1	642273
FAM129A	family with sequence similarity 129, member A	3.5	116496
FAM150B	family with sequence similarity 150, member B	3.4	285016
FAM176A	family with sequence similarity 176, member A	-7.8	84141
FAM198A	family with sequence similarity 198, member A	-5.1	729085
FAM20A	family with sequence similarity 20, member A	-4.3	54757
FAM26F	family with sequence similarity 26, member F	4.2	441168
FAM3B	family with sequence similarity 3, member B	3.5	54097
FAM46C	family with sequence similarity 46, member C	3.3	54855
FAM49A	family with sequence similarity 49, member A	4.8	81553
FAM59A	family with sequence similarity 59, member A	-3.4	64762
FAM60A	family with sequence similarity 60, member A	3.2	58516
FANCD2	Fanconi anemia, complementation group D2	3.2	2177

FANCI	Fanconi anemia, complementation group I	3.1	55215
FBN1	fibrillin 1	3.1	2200
FCER1G	Fc fragment of IgE, high affinity I, receptor for; gamma polypeptide	5.7	2207
FCGR1B	Fc fragment of IgG, high affinity Ib, receptor (CD64)	3.5	2210
FCGR2A	Fc fragment of IgG, low affinity IIa, receptor (CD32)	4.2	2212
FCGR2B	Fc fragment of IgG, low affinity IIb, receptor (CD32)	3.7	2213
FCGR3B	Fc fragment of IgG, low affinity IIIb, receptor (CD16b)	4.2	2215
FCN1	ficolin (collagen/fibrinogen domain containing) 1	4.0	2219
FCRL5	Fc receptor-like 5	10.6	83416
FDX1	ferredoxin 1	-3.3	2230
FER1L4	fer-1-like 4 (C. elegans) pseudogene	6.0	80307
FERMT1	fermitin family member 1	3.1	55612
FERMT3	fermitin family member 3	3.4	83706
FETUB	fetuin B	-4.7	26998
FGA	fibrinogen alpha chain	-10.8	2243
FGB	fibrinogen beta chain	-29.5	2244
FGD2	FYVE, RhoGEF and PH domain containing 2	4.6	221472
FGD3	FYVE, RhoGEF and PH domain containing 3	4.6	89846
FGF1	fibroblast growth factor 1 (acidic)	3.3	2246
FGGY	FGGY carbohydrate kinase domain containing	-3.9	55277
FGL1	fibrinogen-like 1	-10.8	2267
FGL2	fibrinogen-like 2	4.1	10875
FGR	Gardner-Rasheed feline sarcoma viral (v-fgr) oncogene homolog	3.6	2268
FLJ32255	hypothetical LOC643977	3.8	643977
FLNA	filamin A, alpha	3.0	2316
FMNL2	formin-like 2	5.2	114793
FMO3	flavin containing monooxygenase 3	-5.5	2328
FMO5	flavin containing monooxygenase 5	-5.7	2330
FNDC1	fibronectin type III domain containing 1	4.3	84624
FOLH1	folate hydrolase (prostate-specific membrane antigen) 1	-7.8	2346
FOLH1B	folate hydrolase 1B	-6.3	219595
FOLR2	folate receptor 2 (fetal)	6.2	2350
FOXA1	forkhead box A1	-4.8	3169
FOXA3	forkhead box A3	-7.2	3171
FPR3	formyl peptide receptor 3	5.1	2359
FRAS1	Fraser syndrome 1	3.6	80144
FST	follistatin	-5.8	10468
FSTL1	follistatin-like 1	3.0	11167
FTCD	formiminotransferase cyclodeaminase	-4.6	10841
FUT8	fucosyltransferase 8 (alpha (1,6) fucosyltransferase)	3.3	2530
FXYD2	FXYD domain containing ion transport regulator 2	5.2	486
FXYD5	FXYD domain containing ion transport regulator 5	4.3	53827
FYB	FYN binding protein	4.9	2533
FZD2	frizzled family receptor 2	3.1	2535
FZD5	frizzled family receptor 5	-4.0	7855
G6PC	glucose-6-phosphatase, catalytic subunit	-4.0	2538
GABRP	gamma-aminobutyric acid (GABA) A receptor, pi	7.4	2568
GADD45G	growth arrest and DNA-damage-inducible, gamma	-6.0	10912
GAS2	growth arrest-specific 2	-4.6	2620
GAS7	growth arrest-specific 7	4.1	8522
GATM	glycine amidinotransferase (L-arginine:glycine amidinotransferase)	-3.6	2628
GBA3	glucosidase, beta, acid 3 (cytosolic)	-7.3	57733
GBP5	guanylate binding protein 5	3.6	115362
GCDH	glutaryl-CoA dehydrogenase	-3.4	2639
GCGR	glucagon receptor	-3.3	2642
GCH1	GTP cyclohydrolase 1	-3.4	2643

GCKR	glucokinase (hexokinase 4) regulator	-3.1	2646
GCSH	glycine cleavage system protein H (aminomethyl carrier)	-3.3	2653
GFRA1	GDNF family receptor alpha 1	-4.1	2674
GGCX	gamma-glutamyl carboxylase	-4.4	2677
GGH	gamma-glutamyl hydrolase (conjugase, folylpolygammaglutamyl hydrolase)	-7.3	8836
GGTA1P	glycoprotein, alpha-galactosyltransferase 1 pseudogene	4.9	2681
GHR	growth hormone receptor	-14.3	2690
GIMAP1	GTPase, IMAP family member 1	4.1	170575
GIMAP4	GTPase, IMAP family member 4	3.4	55303
GIMAP7	GTPase, IMAP family member 7	4.1	168537
GJA4	gap junction protein, alpha 4, 37kDa	4.2	2701
GJB1	gap junction protein, beta 1, 32kDa	-3.3	2705
GJB2	gap junction protein, beta 2, 26kDa	-8.3	2706
GLCCI1	glucocorticoid induced transcript 1	4.2	113263
GLDC	glycine dehydrogenase (decarboxylating)	-3.9	2731
GLIPR1	GLI pathogenesis-related 1	3.6	11010
GLS2	glutaminase 2 (liver, mitochondrial)	-8.1	27165
GLT1D1	glycosyltransferase 1 domain containing 1	-3.3	144423
GLUD1	glutamate dehydrogenase 1	-5.1	2746
GLUD2	glutamate dehydrogenase 2	-4.2	2747
GLYAT	glycine-N-acyltransferase	-5.1	10249
GLYATL1	glycine-N-acyltransferase-like 1	-11.4	92292
GLYCTK	glycerate kinase	-3.0	132158
GM2A	GM2 ganglioside activator	3.5	2760
GMFG	glia maturation factor, gamma	4.3	9535
GNE	glucosamine (UDP-N-acetyl)-2-epimerase/N-acetylmannosamine kinase	-7.3	10020
GNLY	granulysin	5.7	10578
GNMT	glycine N-methyltransferase	-33.7	27232
GOLIM4	golgi integral membrane protein 4	-3.2	27333
GOLT1A	golgi transport 1A	-4.0	127845
GOT1	glutamic-oxaloacetic transaminase 1, soluble (aspartate aminotransferase 1)	-4.6	2805
GPAM	glycerol-3-phosphate acyltransferase, mitochondrial	-8.7	57678
GPHN	gephyrin	-3.2	10243
GPLD1	glycosylphosphatidylinositol specific phospholipase D1	-3.8	2822
GPNMB	glycoprotein (transmembrane) nmb	10.2	10457
GPR125	G protein-coupled receptor 125	-4.5	166647
GPR128	G protein-coupled receptor 128	-5.5	84873
GPR137B	G protein-coupled receptor 137B	3.2	7107
GPR171	G protein-coupled receptor 171	8.0	29909
GPR18	G protein-coupled receptor 18	3.2	2841
GPR34	G protein-coupled receptor 34	3.2	2857
GPR37	G protein-coupled receptor 37 (endothelin receptor type B-like)	-9.2	2861
GPR65	G protein-coupled receptor 65	3.4	8477
GPR88	G protein-coupled receptor 88	-5.9	54112
GPR98	G protein-coupled receptor 98	-6.7	84059
GPRC5B	G protein-coupled receptor, family C, group 5, member B	3.3	51704
GPX1	glutathione peroxidase 1	3.1	2876
GPX8	glutathione peroxidase 8 (putative)	3.1	493869
GRAMD1C	GRAM domain containing 1C	-4.6	54762
GRB14	growth factor receptor-bound protein 14	-6.9	2888
GREM2	gremlin 2	-4.6	64388
GRHL1	grainyhead-like 1 (Drosophila)	-6.8	29841
GRN	granulin	4.7	2896

GRTP1	growth hormone regulated TBC protein 1	-6.6	79774
GSTP1	glutathione S-transferase pi 1	3.9	2950
GULP1	GULP, engulfment adaptor PTB domain containing 1	3.8	51454
GUSBP11	glucuronidase, beta pseudogene 11	6.6	91316
GVINP1	GTPase, very large interferon inducible pseudogene 1	4.0	387751
GYG2	glycogenin 2	-5.5	8908
GYS2	glycogen synthase 2 (liver)	-16.2	2998
GZMA	granzyme A (granzyme 1, cytotoxic T-lymphocyte-associated serine esterase 3)	11.6	3001
GZMB	granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	12.7	3002
GZMH	granzyme H (cathepsin G-like 2, protein h-CCPX)	7.1	2999
GZMK	granzyme K (granzyme 3; tryptase II)	5.3	3003
H2AFY	H2A histone family, member Y	3.3	9555
HABP2	hyaluronan binding protein 2	-3.8	3026
HAL	histidine ammonia-lyase	-25.1	3034
HAMP	hepcidin antimicrobial peptide	-14.0	57817
HAO1	hydroxyacid oxidase (glycolate oxidase) 1	-13.3	54363
HAO2	hydroxyacid oxidase 2 (long chain)	-16.5	51179
HAVCR2	hepatitis A virus cellular receptor 2	5.8	84868
HCK	hemopoietic cell kinase	4.5	3055
HCLS1	hematopoietic cell-specific Lyn substrate 1	5.5	3059
HCST	hematopoietic cell signal transducer	3.5	10870
HEPH	hephaestin	4.9	9843
HEYL	hairy/enhancer-of-split related with YRPW motif-like	4.4	26508
HFE2	hemochromatosis type 2 (juvenile)	-14.0	148738
HGD	homogentisate 1,2-dioxygenase	-4.2	3081
HGFAC	HGF activator	-4.7	3083
HIBADH	3-hydroxyisobutyrate dehydrogenase	-3.2	11112
HIGD1A	HIG1 hypoxia inducible domain family, member 1A	-3.1	25994
HK1	hexokinase 1	3.1	3098
HLA-DMA	major histocompatibility complex, class II, DM alpha	9.8	3108
HLA-DMB	major histocompatibility complex, class II, DM beta	6.0	3109
HLA-DOA	major histocompatibility complex, class II, DO alpha	8.1	3111
HLA-DPA1	major histocompatibility complex, class II, DP alpha 1	6.3	3113
HLA-DPB1	major histocompatibility complex, class II, DP beta 1	8.7	3115
HLA-DQA1	major histocompatibility complex, class II, DQ alpha 1	14.4	3117
HLA-DQB1	major histocompatibility complex, class II, DQ beta 1	7.3	3119
HLA-DRA	major histocompatibility complex, class II, DR alpha	7.2	3122
HLA-DRB6	major histocompatibility complex, class II, DR beta 6 (pseudogene)	3.0	3128
HLF	hepatic leukemia factor	-3.6	3131
HMCN1	hemicentin 1	3.4	83872
HMGCS2	3-hydroxy-3-methylglutaryl-CoA synthase 2 (mitochondrial)	-11.7	3158
HMHA1	histocompatibility (minor) HA-1	4.2	23526
HMOX1	heme oxygenase (decycling) 1	3.9	3162
HNF4A	hepatocyte nuclear factor 4, alpha	-5.1	3172
HNF4G	hepatocyte nuclear factor 4, gamma	-3.3	3174
HOOK1	hook homolog 1 (Drosophila)	-4.6	51361
HOPX	HOP homeobox	4.3	84525
HPD	4-hydroxyphenylpyruvate dioxygenase	-5.4	3242
HPGD	hydroxyprostaglandin dehydrogenase 15-(NAD)	-11.7	3248
HPN	hepsin	-10.0	3249
HPR	haptoglobin-related protein	-24.2	3250
HPX	hemopexin	-32.7	3263
HRG	histidine-rich glycoprotein	-13.7	3273
HRSP12	heat-responsive protein 12	-6.4	10247

HS3ST1	heparan sulfate (glucosamine) 3-O-sulfotransferase 1	3.8	9957
HS3ST2	heparan sulfate (glucosamine) 3-O-sulfotransferase 2	3.4	9956
HSD11B1	hydroxysteroid (11-beta) dehydrogenase 1	-6.8	3290
HSD17B6	hydroxysteroid (17-beta) dehydrogenase 6 homolog (mouse)	-53.4	8630
HSPA2	heat shock 70kDa protein 2	4.0	3306
HYAL1	hyaluronoglucosaminidase 1	-3.4	3373
ICAM2	intercellular adhesion molecule 2	3.0	3384
ID2	inhibitor of DNA binding 2, dominant negative helix-loop-helix protein	-3.1	3398
IDI1	isopentenyl-diphosphate delta isomerase 1	-3.2	3422
IFI16	interferon, gamma-inducible protein 16	4.2	3428
IFI27	interferon, alpha-inducible protein 27	5.8	3429
IFI30	interferon, gamma-inducible protein 30	4.4	10437
IFITM10	interferon induced transmembrane protein 10	3.4	402778
IGF1	insulin-like growth factor 1 (somatomedin C)	-6.3	3479
IGF2BP3	insulin-like growth factor 2 mRNA binding protein 3	3.3	10643
IGFALS	insulin-like growth factor binding protein, acid labile subunit	-3.2	3483
IGFBP1	insulin-like growth factor binding protein 1	-11.0	3484
IGFBP2	insulin-like growth factor binding protein 2, 36kDa	-4.8	3485
IGHD	immunoglobulin heavy constant delta	5.3	3495
IGHM	immunoglobulin heavy constant mu	12.5	3507
IGJ	immunoglobulin J polypeptide, linker protein for immunoglobulin alpha and mu polypeptides	15.6	3512
IGKC	immunoglobulin kappa constant	13.0	3514
IGKV1-5	immunoglobulin kappa variable 1-5	11.9	28299
IGKV4-1	immunoglobulin kappa variable 4-1	7.3	28908
IGL@	immunoglobulin lambda locus	4.0	3535
IGLJ3	immunoglobulin lambda joining 3	5.5	28831
IGLL3P	immunoglobulin lambda-like polypeptide 3, pseudogene	10.1	91353
IGSF6	immunoglobulin superfamily, member 6	6.8	10261
IL10RA	interleukin 10 receptor, alpha	6.6	3587
IL12RB1	interleukin 12 receptor, beta 1	3.0	3594
IL17RB	interleukin 17 receptor B	-3.3	55540
IL18	interleukin 18 (interferon-gamma-inducing factor)	8.1	3606
IL1RAP	interleukin 1 receptor accessory protein	-10.0	3556
IL1RL1	interleukin 1 receptor-like 1	3.4	9173
IL1RN	interleukin 1 receptor antagonist	-4.1	3557
IL21R	interleukin 21 receptor	3.4	50615
IL28RA	interleukin 28 receptor, alpha (interferon, lambda receptor)	-3.2	163702
IL7R	interleukin 7 receptor	7.1	3575
INHBA	inhibin, beta A	-3.4	3624
INHBE	inhibin, beta E	-18.0	83729
INPP5D	inositol polyphosphate-5-phosphatase, 145kDa	3.7	3635
INSIG1	insulin induced gene 1	-7.8	3638
IPCEF1	interaction protein for cytohesin exchange factors 1	3.7	26034
IPW	imprinted in Prader-Willi syndrome (non-protein coding)	3.3	3653
IQGAP1	IQ motif containing GTPase activating protein 1	3.4	8826
IRAK3	interleukin-1 receptor-associated kinase 3	3.5	11213
ISG20	interferon stimulated exonuclease gene 20kDa	4.1	3669
ISM1	isthmin 1 homolog (zebrafish)	-6.5	140862
ISOC1	isochorismatase domain containing 1	-4.6	51015
ITCH	itchy E3 ubiquitin protein ligase homolog (mouse)	-4.4	83737
ITGA2	integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)	7.8	3673
ITGAL	integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated antigen 1; alpha polypeptide)	3.8	3683
ITGB2	integrin, beta 2 (complement component 3 receptor 3 and 4 subunit)	4.4	3689

ITGB6	integrin, beta 6	3.8	3694
ITGB8	integrin, beta 8	4.2	3696
ITGBL1	integrin, beta-like 1 (with EGF-like repeat domains)	4.4	9358
ITIH1	inter-alpha (globulin) inhibitor H1	-19.5	3697
ITIH2	inter-alpha (globulin) inhibitor H2	-6.3	3698
ITIH3	inter-alpha (globulin) inhibitor H3	-9.3	3699
ITIH4	inter-alpha (globulin) inhibitor H4 (plasma Kallikrein-sensitive glycoprotein)	-6.5	3700
ITK	IL2-inducible T-cell kinase	4.1	3702
ITLN1	intelectin 1 (galactofuranose binding)	4.3	55600
ITM2A	integral membrane protein 2A	3.5	9452
ITM2C	integral membrane protein 2C	3.3	81618
JAK3	Janus kinase 3	4.6	3718
JMJD5	jumonji domain containing 5	-3.5	79831
KANK4	KN motif and ankyrin repeat domains 4	-3.4	163782
KBTBD11	kelch repeat and BTB (POZ) domain containing 11	-3.4	9920
KCNA3	potassium voltage-gated channel, shaker-related subfamily, member 3	3.2	3738
KCND3	potassium voltage-gated channel, Shal-related subfamily, member 3	-6.1	3752
KCNJ16	potassium inwardly-rectifying channel, subfamily J, member 16	3.2	3773
KCNN2	potassium intermediate/small conductance calcium-activated channel, subfamily N, member 2	-8.9	3781
KCNT2	potassium channel, subfamily T, member 2	-3.6	343450
KCTD12	potassium channel tetramerisation domain containing 12	3.4	115207
KDM4C	lysine (K)-specific demethylase 4C	-4.8	23081
KDSR	3-ketodihydrosphingosine reductase	-3.1	2531
KHK	ketohexokinase (fructokinase)	-5.1	3795
KIAA0101	KIAA0101	3.6	9768
KIAA0125	KIAA0125	6.7	9834
KIAA0226	KIAA0226	3.1	9711
KIF11	kinesin family member 11	4.4	3832
KIF16B	kinesin family member 16B	-3.0	55614
KIF21A	kinesin family member 21A	-3.2	55605
KIF4A	kinesin family member 4A	3.3	24137
KLB	klotho beta	-12.1	152831
KLF15	Kruppel-like factor 15	-4.3	28999
KLF5	Kruppel-like factor 5 (intestinal)	3.0	688
KLHL6	kelch-like 6 (Drosophila)	5.7	89857
KLKB1	kallikrein B, plasma (Fletcher factor) 1	-10.8	3818
KLRB1	killer cell lectin-like receptor subfamily B, member 1	3.5	3820
KLRK1	killer cell lectin-like receptor subfamily K, member 1	5.5	22914
KNG1	kininogen 1	-18.5	3827
KRT19	keratin 19	51.4	3880
KRT23	keratin 23 (histone deacetylase inducible)	16.9	25984
KRT7	keratin 7	20.7	3855
LACTB2	lactamase, beta 2	-3.6	51110
LAIR1	leukocyte-associated immunoglobulin-like receptor 1	3.7	3903
LAMA2	laminin, alpha 2	3.2	3908
LAMB1	laminin, beta 1	4.1	3912
LAMC2	laminin, gamma 2	3.7	3918
LAPTM5	lysosomal protein transmembrane 5	5.3	7805
LARP1B	La ribonucleoprotein domain family, member 1B	-4.2	55132
LAX1	lymphocyte transmembrane adaptor 1	5.2	54900
LAYN	layilin	3.2	143903
LBH	limb bud and heart development homolog (mouse)	3.5	81606
LBP	lipopolysaccharide binding protein	-18.0	3929

LCAT	lecithin-cholesterol acyltransferase	-4.4	3931
LCK	lymphocyte-specific protein tyrosine kinase	4.1	3932
LDHB	lactate dehydrogenase B	4.2	3945
LDHD	lactate dehydrogenase D	-4.1	197257
LDLR	low density lipoprotein receptor	-5.9	3949
LEAP2	liver expressed antimicrobial peptide 2	-9.7	116842
LECT2	leukocyte cell-derived chemotaxin 2	-14.2	3950
LEF1	lymphoid enhancer-binding factor 1	3.4	51176
LEPR	leptin receptor	-4.0	3953
LGALS1	lectin, galactoside-binding, soluble, 1	5.4	3956
LGALS3	lectin, galactoside-binding, soluble, 3	3.4	3958
LGALS3BP	lectin, galactoside-binding, soluble, 3 binding protein	3.5	3959
LGMN	legumain	3.0	5641
LGR4	leucine-rich repeat containing G protein-coupled receptor 4	-7.9	55366
LILRA2	leukocyte immunoglobulin-like receptor, subfamily A (with TM domain), member 2	3.1	11027
LILRB1	leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 1	5.4	10859
LILRB2	leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 2	6.9	10288
LINC00261	long intergenic non-protein coding RNA 261	-4.5	140828
LINC00342	long intergenic non-protein coding RNA 342	3.6	150759
LIPC	lipase, hepatic	-10.1	3990
LIPG	lipase, endothelial	-6.4	9388
LMAN1	lectin, mannose-binding, 1	-3.1	3998
LNX2	ligand of numb-protein X 2	-3.3	222484
LOC100130232	LP2209	-7.3	1E+08
LOC100131541	hypothetical LOC100131541	3.7	1E+08
LOC100132741	hypothetical LOC100132741	3.1	1E+08
LOC100288911	hypothetical LOC100288911	4.5	1E+08
LOC100505650	hypothetical LOC100505650	4.7	1.01E+08
LOC100505746	hypothetical LOC100505746	5.6	1.01E+08
LOC100506229	hypothetical LOC100506229	-12.0	1.01E+08
LOC100506776	hypothetical LOC100506776	4.3	1.01E+08
LOC100507307	hypothetical LOC100507307	3.1	1.01E+08
LOC100507389	hypothetical LOC100507389	-8.7	1.01E+08
LOC100509635	hypothetical LOC100509635	3.1	1.01E+08
LOC149703	hypothetical LOC149703	-5.1	149703
LOC153682	hypothetical protein LOC153682	3.4	153682
LOC200772	hypothetical LOC200772	3.9	200772
LOC203274	hypothetical protein LOC203274	3.4	203274
LOC255167	hypothetical LOC255167	-3.6	255167
LOC283587	hypothetical protein LOC283587	-4.2	283587
LOC401522	hypothetical LOC401522	3.4	401522
LOC96610	BMS1 homolog, ribosome assembly protein (yeast) pseudogene	8.1	96610
LONP2	lon peptidase 2, peroxisomal	-3.2	83752
LONRF3	LON peptidase N-terminal domain and ring finger 3	-3.6	79836
LOX	lysyl oxidase	3.0	4015
LOXL1	lysyl oxidase-like 1	3.4	4016
LOXL2	lysyl oxidase-like 2	4.7	4017
LPA	lipoprotein, Lp(a)	-51.9	4018
LPCAT1	lysophosphatidylcholine acyltransferase 1	3.4	79888
LPCAT3	lysophosphatidylcholine acyltransferase 3	-3.7	10162
LPPR1	lipid phosphate phosphatase-related protein type 1	-3.1	54886
LRG1	leucine-rich alpha-2-glycoprotein 1	-17.1	116844
LRIG1	leucine-rich repeats and immunoglobulin-like domains 1	-7.7	26018

LRP6	low density lipoprotein receptor-related protein 6	-3.3	4040
LRRC1	leucine rich repeat containing 1	3.3	55227
LRRC2	leucine rich repeat containing 2	-3.0	79442
LST1	leukocyte specific transcript 1	4.0	7940
LUM	lumican	7.3	4060
LXN	latexin	9.1	56925
LY75	lymphocyte antigen 75	4.0	4065
LY86	lymphocyte antigen 86	4.7	9450
LY9	lymphocyte antigen 9	3.2	4063
LY96	lymphocyte antigen 96	7.1	23643
LYZ	lysozyme	5.9	4069
MAD2L1	MAD2 mitotic arrest deficient-like 1 (yeast)	3.5	4085
MAML2	mastermind-like 2 (Drosophila)	4.3	84441
MAN1A1	mannosidase, alpha, class 1A, member 1	-4.2	4121
MANEA	mannosidase, endo-alpha	-3.2	79694
MAOA	monoamine oxidase A	-4.8	4128
MAP1B	microtubule-associated protein 1B	3.0	4131
MAP2	microtubule-associated protein 2	3.4	4133
MAP3K8	mitogen-activated protein kinase kinase kinase 8	3.6	1326
MAP4K1	mitogen-activated protein kinase kinase kinase kinase 1	3.1	11184
MAP7	microtubule-associated protein 7	-3.2	9053
MAPK13	mitogen-activated protein kinase 13	3.6	5603
MARCH1	membrane-associated ring finger (C3HC4) 1	4.7	55016
MARCO	macrophage receptor with collagenous structure	5.2	8685
MASP2	mannan-binding lectin serine peptidase 2	-8.8	10747
MAT1A	methionine adenosyltransferase I, alpha	-14.9	4143
MBL2	mannose-binding lectin (protein C) 2, soluble	-29.8	4153
MCC	mutated in colorectal cancers	-4.3	4163
MCFD2	multiple coagulation factor deficiency 2	-3.7	90411
MCM5	minichromosome maintenance complex component 5	3.4	4174
MEG3	maternally expressed 3 (non-protein coding)	3.1	55384
MEGF9	multiple EGF-like-domains 9	-3.3	1955
MELK	maternal embryonic leucine zipper kinase	4.0	9833
MET	met proto-oncogene (hepatocyte growth factor receptor)	-3.2	4233
METRNL	meteorin, glial cell differentiation regulator-like	3.4	284207
MFAP3L	microfibrillar-associated protein 3-like	-19.7	9848
MFI2	antigen p97 (melanoma associated) identified by monoclonal antibodies 133.2 and 96.5	7.0	4241
MFSD2A	major facilitator superfamily domain containing 2A	-5.6	84879
MGP	matrix Gla protein	3.8	4256
MGST1	microsomal glutathione S-transferase 1	-4.7	4257
MICAL1	microtubule associated monoxygenase, calponin and LIM domain containing 1	5.1	64780
MICB	MHC class I polypeptide-related sequence B	4.0	4277
MIR143HG	MIR143 host gene (non-protein coding)	3.4	728264
MIS18BP1	MIS18 binding protein 1	3.3	55320
MKI67	antigen identified by monoclonal antibody Ki-67	3.9	4288
MLIP	muscular LMNA-interacting protein	-5.2	90523
MLXIPL	MLX interacting protein-like	-5.5	51085
MMAA	methylmalonic aciduria (cobalamin deficiency) cblA type	-3.4	166785
MMAB	methylmalonic aciduria (cobalamin deficiency) cblB type	-3.4	326625
MME	membrane metallo-endopeptidase	-5.2	4311
MMP2	matrix metallopeptidase 2 (gelatinase A, 72kDa gelatinase, 72kDa type IV collagenase)	4.8	4313
MMP7	matrix metallopeptidase 7 (matrilysin, uterine)	27.6	4316
MOBKL2A	MOB1, Mps One Binder kinase activator-like 2A (yeast)	3.4	126308

MOCOS	molybdenum cofactor sulfurase	-5.7	55034
MOSC1	MOCO sulphurase C-terminal domain containing 1	-3.3	64757
MOSC2	MOCO sulphurase C-terminal domain containing 2	-7.8	54996
MOXD1	monooxygenase, DBH-like 1	3.7	26002
MPEG1	macrophage expressed 1	6.0	219972
MRAS	muscle RAS oncogene homolog	3.0	22808
MRC2	mannose receptor, C type 2	3.9	9902
MS4A1	membrane-spanning 4-domains, subfamily A, member 1	3.1	931
MS4A14	membrane-spanning 4-domains, subfamily A, member 14	4.8	84689
MS4A4A	membrane-spanning 4-domains, subfamily A, member 4	6.6	51338
MS4A6A	membrane-spanning 4-domains, subfamily A, member 6A	4.4	64231
MS4A7	membrane-spanning 4-domains, subfamily A, member 7	7.0	58475
MSMO1	methylsterol monooxygenase 1	-5.8	6307
MST1	macrophage stimulating 1 (hepatocyte growth factor-like)	-6.5	4485
MST1P9	macrophage stimulating 1 (hepatocyte growth factor-like) pseudogene 9	-4.6	11223
MT1F	metallothionein 1F	-3.6	4494
MT1G	metallothionein 1G	-3.9	4495
MT1H	metallothionein 1H	-3.1	4496
MT1M	metallothionein 1M	-6.7	4499
MT1X	metallothionein 1X	-3.1	4501
MTFR1	mitochondrial fission regulator 1	-3.7	9650
MTHFD1	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1, methenyltetrahydrofolate cyclohydrolase, formyltetrahydrofolate synthetase	-3.3	4522
MTHFD2	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase	4.5	10797
MTHFD2L	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2-like	-4.2	441024
MTHFS	5,10-methenyltetrahydrofolate synthetase (5-formyltetrahydrofolate cyclo-ligase)	-3.9	10588
MTTP	microsomal triglyceride transfer protein	-13.5	4547
MUT	methylmalonyl CoA mutase	-3.7	4594
MX2	myxovirus (influenza virus) resistance 2 (mouse)	3.1	4600
MXRA8	matrix-remodelling associated 8	3.3	54587
MYBL1	v-myb myeloblastosis viral oncogene homolog (avian)-like 1	3.3	4603
MYL9	myosin, light chain 9, regulatory	4.5	10398
MYO10	myosin X	3.2	4651
MYO1B	myosin IB	-3.7	4430
MYO5A	myosin VA (heavy chain 12, myoxin)	3.6	4644
MYOM1	myomesin 1, 185kDa	-6.0	8736
MYRIP	myosin VIIA and Rab interacting protein	-5.7	25924
MZB1	marginal zone B and B1 cell-specific protein	17.6	51237
N4BP2	NEDD4 binding protein 2	-3.9	55728
NADKD1	NAD kinase domain containing 1	-6.8	133686
NAGS	N-acetylglutamate synthase	-3.3	162417
NALCN	sodium leak channel, non-selective	4.0	259232
NAMPT	nicotinamide phosphoribosyltransferase	-4.6	10135
NAT2	N-acetyltransferase 2 (arylamine N-acetyltransferase)	-7.0	10
NCAPG	non-SMC condensin I complex, subunit G	3.6	64151
NCEH1	neutral cholesterol ester hydrolase 1	4.5	57552
NCF1C	neutrophil cytosolic factor 1C pseudogene	4.8	654817
NCF2	neutrophil cytosolic factor 2	5.0	4688
NCF4	neutrophil cytosolic factor 4, 40kDa	4.3	4689
NDC80	NDC80 homolog, kinetochore complex component (S. cerevisiae)	5.0	10403
NEK6	NIMA (never in mitosis gene a)-related kinase 6	-3.3	10783

NEXN	nexilin (F actin binding protein)	4.6	91624
NFIA	nuclear factor I/A	-3.1	4774
NFIL3	nuclear factor, interleukin 3 regulated	-3.2	4783
NGEF	neuronal guanine nucleotide exchange factor	-3.2	25791
NID2	nidogen 2 (osteonidogen)	3.1	22795
NKG7	natural killer cell group 7 sequence	6.0	4818
NLRC3	NLR family, CARD domain containing 3	4.1	197358
NLRC4	NLR family, CARD domain containing 4	4.7	58484
NNMT	nicotinamide N-methyltransferase	-4.9	4837
NNT	nicotinamide nucleotide transhydrogenase	-3.3	23530
NPC2	Niemann-Pick disease, type C2	3.7	10577
NPL	N-acetylneuraminate pyruvate lyase (dihydrodipicolinate synthase)	4.8	80896
NPNT	nephronectin	3.6	255743
NQO1	NAD(P)H dehydrogenase, quinone 1	8.4	1728
NR0B2	nuclear receptor subfamily 0, group B, member 2	-3.4	8431
NR1I2	nuclear receptor subfamily 1, group I, member 2	-5.6	8856
NR1I3	nuclear receptor subfamily 1, group I, member 3	-7.5	9970
NR5A2	nuclear receptor subfamily 5, group A, member 2	-5.5	2494
NRTN	neurturin	-4.3	4902
NSUN6	NOP2/Sun domain family, member 6	-4.5	221078
NT5DC2	5'-nucleotidase domain containing 2	3.6	64943
NUDT7	nudix (nucleoside diphosphate linked moiety X)-type motif 7	-4.2	283927
ODZ1	odz, odd Oz/ten-m homolog 1 (Drosophila)	-15.7	10178
OGDHL	oxoglutarate dehydrogenase-like	-6.2	55753
ORAI2	ORAI calcium release-activated calcium modulator 2	3.3	80228
ORM1	orosomucoid 1	-53.0	5004
OSBPL3	oxysterol binding protein-like 3	6.2	26031
OSBPL8	oxysterol binding protein-like 8	3.5	114882
OSTalpha	organic solute transporter alpha	-3.9	200931
OTC	ornithine carbamoyltransferase	-4.5	5009
P2RX5	purinergic receptor P2X, ligand-gated ion channel, 5	4.9	5026
P2RY12	purinergic receptor P2Y, G-protein coupled, 12	7.9	64805
P2RY13	purinergic receptor P2Y, G-protein coupled, 13	3.6	53829
P2RY8	purinergic receptor P2Y, G-protein coupled, 8	5.1	286530
PAH	phenylalanine hydroxylase	-4.4	5053
PAIP2B	poly(A) binding protein interacting protein 2B	-3.7	400961
PALLD	palladin, cytoskeletal associated protein	3.0	23022
PALM2	paralemmin 2	-10.1	114299
PAMR1	peptidase domain containing associated with muscle regeneration 1	3.3	25891
PANK1	pantothenate kinase 1	-7.8	53354
PAPLN	papilin, proteoglycan-like sulfated glycoprotein	6.6	89932
PAQR5	progestin and adipoQ receptor family member V	4.3	54852
PAQR8	progestin and adipoQ receptor family member VIII	3.0	85315
PAQR9	progestin and adipoQ receptor family member IX	-10.7	344838
PAX5	paired box 5	3.2	5079
PBLD	phenazine biosynthesis-like protein domain containing	-6.0	64081
PC	pyruvate carboxylase	-9.0	5091
PCCB	propionyl CoA carboxylase, beta polypeptide	-3.2	5096
PCK1	phosphoenolpyruvate carboxykinase 1 (soluble)	-9.6	5105
PCOLCE2	procollagen C-endopeptidase enhancer 2	-10.5	26577
PCSK6	proprotein convertase subtilisin/kexin type 6	-14.4	5046
PCSK9	proprotein convertase subtilisin/kexin type 9	-5.0	255738
PCYOX1L	prenylcysteine oxidase 1 like	3.1	78991
PDE11A	phosphodiesterase 11A	-5.4	50940
PDE1A	phosphodiesterase 1A, calmodulin-dependent	3.3	5136
PDE4A	phosphodiesterase 4A, cAMP-specific	3.1	5141

PDIA5	protein disulfide isomerase family A, member 5	-3.2	10954
PDZK1IP1	PDZK1 interacting protein 1	3.8	10158
PECAM1	platelet/endothelial cell adhesion molecule	4.0	5175
PER2	period homolog 2 (Drosophila)	-3.1	8864
PEX13	peroxisomal biogenesis factor 13	-3.5	5194
PFKFB1	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 1	-3.9	5207
PFKFB3	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3	3.4	5209
PFKP	phosphofructokinase, platelet	5.0	5214
PGLYRP2	peptidoglycan recognition protein 2	-12.3	114770
PGM1	phosphoglucomutase 1	-4.7	5236
PGRMC1	progesterone receptor membrane component 1	-5.4	10857
PHYH	phytanoyl-CoA 2-hydroxylase	-3.6	5264
PID1	phosphotyrosine interaction domain containing 1	-7.1	55022
PIK3C2G	phosphoinositide-3-kinase, class 2, gamma polypeptide	-4.4	5288
PIK3CD	phosphoinositide-3-kinase, catalytic, delta polypeptide	3.6	5293
PIK3IP1	phosphoinositide-3-kinase interacting protein 1	3.2	113791
PIK3R5	phosphoinositide-3-kinase, regulatory subunit 5	4.7	23533
PILRA	paired immunoglobin-like type 2 receptor alpha	3.5	29992
PIM2	pim-2 oncogene	3.6	11040
PIPOX	pipecolic acid oxidase	-7.3	51268
PKIB	protein kinase (cAMP-dependent, catalytic) inhibitor beta	3.6	5570
PKM2	pyruvate kinase, muscle	3.1	5315
PKP2	plakophilin 2	-4.7	5318
PLA1A	phospholipase A1 member A	-3.3	51365
PLA2G12B	phospholipase A2, group XIIB	-4.8	84647
PLA2G7	phospholipase A2, group VII (platelet-activating factor acetylhydrolase, plasma)	13.6	7941
PLAT	plasminogen activator, tissue	3.3	5327
PLD3	phospholipase D family, member 3	3.0	23646
PLG	plasminogen	-16.9	5340
PLGLB2	plasminogen-like B2	-10.1	5342
PLIN5	perilipin 5	-3.2	440503
PLP2	proteolipid protein 2 (colonic epithelium-enriched)	3.4	5355
PLSCR4	phospholipid scramblase 4	-3.1	57088
PLTP	phospholipid transfer protein	8.7	5360
PLXDC2	plexin domain containing 2	3.6	84898
PLXNA1	plexin A1	3.7	5361
PLXNC1	plexin C1	4.9	10154
PMEPA1	prostate transmembrane protein, androgen induced 1	5.1	56937
PMP22	peripheral myelin protein 22	3.0	5376
PNOC	prepronociceptin	4.9	5368
PNPLA3	patatin-like phospholipase domain containing 3	-6.8	80339
POM121L9P	POM121 membrane glycoprotein-like 9, pseudogene	5.7	29774
PON1	paraoxonase 1	-17.1	5444
PON3	paraoxonase 3	-17.0	5446
POU2AF1	POU class 2 associating factor 1	31.8	5450
PPAP2C	phosphatidic acid phosphatase type 2C	3.2	8612
PPID	peptidylprolyl isomerase D	-4.4	5481
PPP1R14A	protein phosphatase 1, regulatory (inhibitor) subunit 14A	4.2	94274
PPP1R1A	protein phosphatase 1, regulatory (inhibitor) subunit 1A	-9.4	5502
PPP1R3B	protein phosphatase 1, regulatory (inhibitor) subunit 3B	-3.2	79660
PPP1R3C	protein phosphatase 1, regulatory (inhibitor) subunit 3C	-7.8	5507
PPP2R1B	protein phosphatase 2, regulatory subunit A, beta	-7.3	5519
PPT1	palmitoyl-protein thioesterase 1	3.6	5538
PRC1	protein regulator of cytokinesis 1	5.1	9055
PRDM1	PR domain containing 1, with ZNF domain	6.5	639

PRDX3	peroxiredoxin 3	-3.3	10935
PRELP	proline/arginine-rich end leucine-rich repeat protein	3.1	5549
PRF1	perforin 1 (pore forming protein)	5.6	5551
PRG4	proteoglycan 4	-11.9	10216
PRKCB	protein kinase C, beta	3.8	5579
PRKX	protein kinase, X-linked	3.8	5613
PROC	protein C (inactivator of coagulation factors Va and VIIIa)	-6.7	5624
PROCR	protein C receptor, endothelial	4.7	10544
PROM1	prominin 1	5.2	8842
PROX1	prospero homeobox 1	-3.6	5629
PROZ	protein Z, vitamin K-dependent plasma glycoprotein	-4.0	8858
PRR11	proline rich 11	7.1	55771
PRRG4	proline rich Gla (G-carboxyglutamic acid) 4 (transmembrane)	-5.0	79056
PRSS23	protease, serine, 23	4.4	11098
PSAT1	phosphoserine aminotransferase 1	-4.0	29968
PTAFR	platelet-activating factor receptor	3.4	5724
PTGDR	prostaglandin D2 receptor (DP)	4.6	5729
PTGDS	prostaglandin D2 synthase 21kDa (brain)	3.0	5730
PTGIS	prostaglandin I2 (prostacyclin) synthase	3.5	5740
PTGR1	prostaglandin reductase 1	-3.1	22949
PTP4A1	protein tyrosine phosphatase type IVA, member 1	-4.3	7803
PTPLAD2	protein tyrosine phosphatase-like A domain containing 2	3.5	401494
PTPN22	protein tyrosine phosphatase, non-receptor type 22 (lymphoid)	3.6	26191
PTPN3	protein tyrosine phosphatase, non-receptor type 3	-6.0	5774
PTPRC	protein tyrosine phosphatase, receptor type, C	4.2	5788
PTPRF	protein tyrosine phosphatase, receptor type, F	-4.8	5792
PTTG1	pituitary tumor-transforming 1	3.7	9232
PVRIG	poliovirus receptor related immunoglobulin domain containing	3.6	79037
PVRL3	poliovirus receptor-related 3	-5.1	25945
PXMP2	peroxisomal membrane protein 2, 22kDa	-5.1	5827
PYCARD	PYD and CARD domain containing	4.1	29108
PYHIN1	pyrin and HIN domain family, member 1	5.3	149628
PZP	pregnancy-zone protein	-11.1	5858
RAB14	RAB14, member RAS oncogene family	-3.0	51552
RAB17	RAB17, member RAS oncogene family	-3.9	64284
RAB25	RAB25, member RAS oncogene family	4.1	57111
RAB27A	RAB27A, member RAS oncogene family	-3.8	5873
RAB31	RAB31, member RAS oncogene family	4.8	11031
RAB34	RAB34, member RAS oncogene family	3.9	83871
RAB7B	RAB7B, member RAS oncogene family	3.5	338382
RABGAP1L	RAB GTPase activating protein 1-like	3.6	9910
RAC2	ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2)	4.8	5880
RACGAP1	Rac GTPase activating protein 1	5.8	29127
RAPGEF4	Rap guanine nucleotide exchange factor (GEF) 4	-3.5	11069
RARRES2	retinoic acid receptor responder (tazarotene induced) 2	-3.8	5919
RASEF	RAS and EF-hand domain containing	5.3	158158
RASGRP1	RAS guanyl releasing protein 1 (calcium and DAG-regulated)	7.1	10125
RASSF2	Ras association (RalGDS/AF-6) domain family member 2	3.1	9770
RASSF4	Ras association (RalGDS/AF-6) domain family member 4	3.4	83937
RBMS2	RNA binding motif, single stranded interacting protein 2	3.1	5939
RBP1	retinol binding protein 1, cellular	3.8	5947
RBP4	retinol binding protein 4, plasma	-5.5	5950
RBP7	retinol binding protein 7, cellular	3.7	116362
RCL1	RNA terminal phosphate cyclase-like 1	-3.4	10171
RCSD1	RCSD domain containing 1	6.0	92241

RDH10	retinol dehydrogenase 10 (all-trans)	-3.5	157506
RDH11	retinol dehydrogenase 11 (all-trans/9-cis/11-cis)	-3.4	51109
RDH16	retinol dehydrogenase 16 (all-trans)	-14.7	8608
REEP6	receptor accessory protein 6	-4.8	92840
REPS2	RALBP1 associated Eps domain containing 2	-3.3	9185
RGL1	ral guanine nucleotide dissociation stimulator-like 1	3.5	23179
RGN	regucalcin (senescence marker protein-30)	-7.3	9104
RGS10	regulator of G-protein signaling 10	5.7	6001
RHOBTB1	Rho-related BTB domain containing 1	5.3	9886
RNASE1	ribonuclease, RNase A family, 1 (pancreatic)	10.6	6035
RNASE2	ribonuclease, RNase A family, 2 (liver, eosinophil-derived neurotoxin)	5.0	6036
RNASE4	ribonuclease, RNase A family, 4	-9.3	6038
RNASE6	ribonuclease, RNase A family, k6	12.6	6039
RNASET2	ribonuclease T2	4.5	8635
RND1	Rho family GTPase 1	-5.5	27289
RNF128	ring finger protein 128	-3.2	79589
RNF135	ring finger protein 135	4.3	84282
RNF165	ring finger protein 165	-3.5	494470
RNFT1	ring finger protein, transmembrane 1	-3.1	51136
RORC	RAR-related orphan receptor C	-5.7	6097
RRM2	ribonucleotide reductase M2	7.1	6241
RTP3	receptor (chemosensory) transporter protein 3	-3.3	83597
RUNDC3B	RUN domain containing 3B	-7.6	154661
RUNX1	runt-related transcription factor 1	3.3	861
RUNX2	runt-related transcription factor 2	4.9	860
RUNX3	runt-related transcription factor 3	5.0	864
RWDD2B	RWD domain containing 2B	-4.0	10069
S100A11	S100 calcium binding protein A11	10.3	6282
S100A12	S100 calcium binding protein A12	3.8	6283
S100A4	S100 calcium binding protein A4	5.4	6275
S100A6	S100 calcium binding protein A6	8.1	6277
S100A9	S100 calcium binding protein A9	3.6	6280
SAA4	serum amyloid A4, constitutive	-20.7	6291
SALL1	sal-like 1 (Drosophila)	-7.6	6299
SAMD3	sterile alpha motif domain containing 3	3.9	154075
SAMD9	sterile alpha motif domain containing 9	3.1	54809
SAMD9L	sterile alpha motif domain containing 9-like	4.0	219285
SAMHD1	SAM domain and HD domain 1	3.7	25939
SAMSN1	SAM domain, SH3 domain and nuclear localization signals 1	3.1	64092
SASH3	SAM and SH3 domain containing 3	4.0	54440
SC5DL	sterol-C5-desaturase (ERG3 delta-5-desaturase homolog, S. cerevisiae)-like	-5.2	6309
SCD	stearoyl-CoA desaturase (delta-9-desaturase)	-4.2	6319
SCD5	stearoyl-CoA desaturase 5	4.4	79966
SCPEP1	serine carboxypeptidase 1	3.3	59342
SCRN1	secernin 1	3.8	9805
SDC2	syndecan 2	-5.7	6383
SDC3	syndecan 3	4.9	9672
SEC14L1	SEC14-like 1 (S. cerevisiae)	3.4	6397
SEC16B	SEC16 homolog B (S. cerevisiae)	-3.3	89866
SEL1L	sel-1 suppressor of lin-12-like (C. elegans)	-3.5	6400
SEL1L3	sel-1 suppressor of lin-12-like 3 (C. elegans)	5.9	23231
SELM	selenoprotein M	4.5	140606
SELPLG	selectin P ligand	6.2	6404
SEMA4D	sema domain, immunoglobulin domain (Ig), transmembrane domain		10507

	(TM) and short cytoplasmic domain, (semaphorin) 4D	3.1	
SEPP1	selenoprotein P, plasma, 1	-3.2	6414
SERINC5	serine incorporator 5	-3.9	256987
SERPINA1	serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1	-5.5	5265
SERPINA10	serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 10	-34.6	51156
SERPINA3	serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 3	-3.7	12
SERPINA4	serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 4	-3.0	5267
SERPINA5	serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 5	-3.1	5104
SERPINA6	serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 6	-6.4	866
SERPINA7	serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 7	-25.2	6906
SERPINC1	serpin peptidase inhibitor, clade C (antithrombin), member 1	-28.4	462
SERPIND1	serpin peptidase inhibitor, clade D (heparin cofactor), member 1	-27.1	3053
SERPINE2	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 2	4.7	5270
SERPINF1	serpin peptidase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 1	-4.5	5176
SERPINF2	serpin peptidase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 2	-10.0	5345
SFN	stratifin	6.4	2810
SGK2	serum/glucocorticoid regulated kinase 2	-3.9	10110
SGK223	homolog of rat pragma of Rnd2	4.2	157285
SGPP2	sphingosine-1-phosphate phosphatase 2	5.1	130367
SH2D1A	SH2 domain containing 1A	3.4	4068
SH3BGRL3	SH3 domain binding glutamic acid-rich protein like 3	4.3	83442
SHMT1	serine hydroxymethyltransferase 1 (soluble)	-5.4	6470
SIDT1	SID1 transmembrane family, member 1	3.1	54847
SIGLEC1	sialic acid binding Ig-like lectin 1, sialoadhesin	5.8	6614
SIGLEC10	sialic acid binding Ig-like lectin 10	4.5	89790
SIGLEC11	sialic acid binding Ig-like lectin 11	3.5	114132
SIGLEC7	sialic acid binding Ig-like lectin 7	4.7	27036
SLA	Src-like-adaptor	4.9	6503
SLAMF7	SLAM family member 7	9.3	57823
SLAMF8	SLAM family member 8	5.4	56833
SLC10A1	solute carrier family 10 (sodium/bile acid cotransporter family), member 1	-8.5	6554
SLC12A2	solute carrier family 12 (sodium/potassium/chloride transporters), member 2	4.6	6558
SLC13A5	solute carrier family 13 (sodium-dependent citrate transporter), member 5	-41.7	284111
SLC16A10	solute carrier family 16, member 10 (aromatic amino acid transporter)	-4.3	117247
SLC16A2	solute carrier family 16, member 2 (monocarboxylic acid transporter 8)	-4.0	6567
SLC17A2	solute carrier family 17 (sodium phosphate), member 2	-30.8	10246
SLC19A3	solute carrier family 19, member 3	-4.7	80704
SLC1A1	solute carrier family 1 (neuronal/epithelial high affinity glutamate transporter, system Xag), member 1	-6.6	6505
SLC1A2	solute carrier family 1 (glial high affinity glutamate transporter), member 2	-3.7	6506

SLC1A3	solute carrier family 1 (glial high affinity glutamate transporter), member 3	3.2	6507
SLC22A1	solute carrier family 22 (organic cation transporter), member 1	-20.6	6580
SLC22A25	solute carrier family 22, member 25	-5.1	387601
SLC22A3	solute carrier family 22 (extraneuronal monoamine transporter), member 3	-7.2	6581
SLC22A7	solute carrier family 22 (organic anion transporter), member 7	-6.0	10864
SLC22A9	solute carrier family 22 (organic anion transporter), member 9	-3.3	114571
SLC25A13	solute carrier family 25, member 13 (citrin)	-3.0	10165
SLC25A16	solute carrier family 25 (mitochondrial carrier; Graves disease autoantigen), member 16	-3.6	8034
SLC25A18	solute carrier family 25 (mitochondrial carrier), member 18	-7.1	83733
SLC25A36	solute carrier family 25, member 36	3.9	55186
SLC25A47	solute carrier family 25, member 47	-4.0	283600
SLC27A2	solute carrier family 27 (fatty acid transporter), member 2	-19.7	11001
SLC27A5	solute carrier family 27 (fatty acid transporter), member 5	-11.1	10998
SLC28A1	solute carrier family 28 (sodium-coupled nucleoside transporter), member 1	-3.4	9154
SLC2A10	solute carrier family 2 (facilitated glucose transporter), member 10	-7.3	81031
SLC2A2	solute carrier family 2 (facilitated glucose transporter), member 2	-11.9	6514
SLC2A5	solute carrier family 2 (facilitated glucose/fructose transporter), member 5	4.6	6518
SLC30A1	solute carrier family 30 (zinc transporter), member 1	-5.8	7779
SLC30A10	solute carrier family 30, member 10	-6.4	55532
SLC31A1	solute carrier family 31 (copper transporters), member 1	-3.4	1317
SLC35D1	solute carrier family 35 (UDP-glucuronic acid/UDP-N-acetylgalactosamine dual transporter), member D1	-3.7	23169
SLC38A3	solute carrier family 38, member 3	-3.3	10991
SLC38A4	solute carrier family 38, member 4	-15.3	55089
SLC39A14	solute carrier family 39 (zinc transporter), member 14	-5.5	23516
SLC41A2	solute carrier family 41, member 2	-6.0	84102
SLC44A1	solute carrier family 44, member 1	-3.7	23446
SLC44A2	solute carrier family 44, member 2	3.0	57153
SLC47A1	solute carrier family 47, member 1	-5.8	55244
SLC6A1	solute carrier family 6 (neurotransmitter transporter, GABA), member 1	-23.3	6529
SLC6A12	solute carrier family 6 (neurotransmitter transporter, betaine/GABA), member 12	-3.6	6539
SLC6A6	solute carrier family 6 (neurotransmitter transporter, taurine), member 6	3.5	6533
SLC7A11	solute carrier family 7 (anionic amino acid transporter light chain, xc- system),member 11	4.3	23657
SLC7A2	solute carrier family 7 (cationic amino acid transporter, y+ system), member 2	-4.4	6542
SLC7A7	solute carrier family 7 (amino acid transporter light chain, y+L system), member 7	5.1	9056
SLC7A9	solute carrier family 7 (glycoprotein-associated amino acid transporter light chain, bo,+ system), member 9	-4.8	11136
SLC8A1	solute carrier family 8 (sodium/calcium exchanger), member 1	6.3	6546
SLC9B2	solute carrier family 9, subfamily B (cation proton antiporter 2), member 2	-5.5	133308
SLCO1B1	solute carrier organic anion transporter family, member 1B1	-20.9	10599
SLCO1B3	solute carrier organic anion transporter family, member 1B3	-24.4	28234
SLCO4C1	solute carrier organic anion transporter family, member 4C1	-14.3	353189
SLFN12	schlafen family member 12	3.2	55106
SMEK2	SMEK homolog 2, suppressor of mek1 (Dictyostelium)	-3.0	57223

SMOC1	SPARC related modular calcium binding 1	-3.2	64093
SNX20	sorting nexin 20	4.3	124460
SOCS6	suppressor of cytokine signaling 6	-3.2	9306
SORD	sorbitol dehydrogenase	-3.9	6652
SOX4	SRY (sex determining region Y)-box 4	4.3	6659
SOX9	SRY (sex determining region Y)-box 9	3.7	6662
SP140	SP140 nuclear body protein	4.4	11262
SPATS2	spermatogenesis associated, serine-rich 2	3.5	65244
SPINT1	serine peptidase inhibitor, Kunitz type 1	3.1	6692
SPINT2	serine peptidase inhibitor, Kunitz type, 2	4.9	10653
SPOCK2	sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 2	3.5	9806
SPP1	secreted phosphoprotein 1	10.2	6696
SPP2	secreted phosphoprotein 2, 24kDa	-14.2	6694
SPRYD4	SPRY domain containing 4	-3.0	283377
SRD5A1	steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1)	-3.5	6715
SRD5A2	steroid-5-alpha-reductase, alpha polypeptide 2 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 2)	-7.0	6716
SRPX2	sushi-repeat containing protein, X-linked 2	6.0	27286
SSTR1	somatostatin receptor 1	-5.8	6751
ST3GAL6	ST3 beta-galactoside alpha-2,3-sialyltransferase 6	-9.5	10402
ST6GAL1	ST6 beta-galactosamide alpha-2,6-sialyltranferase 1	-4.5	6480
ST6GAL2	ST6 beta-galactosamide alpha-2,6-sialyltranferase 2	3.9	84620
ST8SIA4	ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 4	4.1	7903
STARD4	StAR-related lipid transfer (START) domain containing 4	-3.9	134429
STEAP3	STEAP family member 3	-6.4	55240
STK10	serine/threonine kinase 10	4.5	6793
STK39	serine threonine kinase 39	4.9	27347
STRADB	STE20-related kinase adaptor beta	-3.4	55437
SUCLG2	succinate-CoA ligase, GDP-forming, beta subunit	-3.0	8801
SULT2A1	sulfotransferase family, cytosolic, 2A, dehydroepiandrosterone (DHEA)-preferring, member 1	-11.2	6822
SUSD2	sushi domain containing 2	8.1	56241
SYBU	syntabulin (syntaxin-interacting)	-5.6	55638
SYK	spleen tyrosine kinase	5.5	6850
SYNPO2	synaptopodin 2	3.2	171024
SYT13	synaptotagmin XIII	8.2	57586
SYT17	synaptotagmin XVII	-5.8	51760
SYTL1	synaptotagmin-like 1	3.5	84958
SYTL2	synaptotagmin-like 2	4.8	54843
SYTL3	synaptotagmin-like 3	4.4	94120
TACSTD2	tumor-associated calcium signal transducer 2	12.4	4070
TAGLN	transgelin	3.7	6876
TAT	tyrosine aminotransferase	-3.0	6898
TBC1D10C	TBC1 domain family, member 10C	3.1	374403
TBC1D8B	TBC1 domain family, member 8B (with GRAM domain)	-3.5	54885
TBX15	T-box 15	-3.9	6913
TBXAS1	thromboxane A synthase 1 (platelet)	3.3	6916
TCEA3	transcription elongation factor A (SII), 3	-4.3	6920
TDO2	tryptophan 2,3-dioxygenase	-4.3	6999
TESC	tescalcin	5.7	54997
TF	transferrin	-3.4	7018
TFB2M	transcription factor B2, mitochondrial	-3.1	64216
TFEC	transcription factor EC	3.9	22797
TFPI	tissue factor pathway inhibitor (lipoprotein-associated coagulation	-3.1	7035

	inhibitor)		
TFR2	transferrin receptor 2	-22.8	7036
TGFB1I1	transforming growth factor beta 1 induced transcript 1	4.3	7041
THBS1	thrombospondin 1	3.3	7057
THBS2	thrombospondin 2	5.8	7058
THRB	thyroid hormone receptor, beta (erythroblastic leukemia viral (v-erb-a) oncogene homolog 2, avian)	-4.5	7068
THRSP	thyroid hormone responsive	-13.7	7069
TIGD2	tigger transposable element derived 2	-3.3	166815
TIMD4	T-cell immunoglobulin and mucin domain containing 4	5.2	91937
TIMP1	TIMP metallopeptidase inhibitor 1	6.0	7076
TLR4	toll-like receptor 4	3.4	7099
TLR8	toll-like receptor 8	4.3	51311
TM4SF5	transmembrane 4 L six family member 5	-4.7	9032
TMC4	transmembrane channel-like 4	3.5	147798
TMC8	transmembrane channel-like 8	3.0	147138
TMED3	transmembrane emp24 protein transport domain containing 3	3.2	23423
TMEM106A	transmembrane protein 106A	3.5	113277
TMEM176A	transmembrane protein 176A	-3.6	55365
TMEM176B	transmembrane protein 176B	-4.7	28959
TMEM220	transmembrane protein 220	-6.5	388335
TMEM38B	transmembrane protein 38B	-3.3	55151
TMEM41B	transmembrane protein 41B	-4.1	440026
TMEM45A	transmembrane protein 45A	-6.1	55076
TMEM97	transmembrane protein 97	-3.2	27346
TMSB10	thymosin beta 10	6.2	9168
TNC	tenascin C	4.4	3371
TNFRSF17	tumor necrosis factor receptor superfamily, member 17	13.7	608
TNFRSF19	tumor necrosis factor receptor superfamily, member 19	3.0	55504
TNFRSF21	tumor necrosis factor receptor superfamily, member 21	3.0	27242
TNFSF13B	tumor necrosis factor (ligand) superfamily, member 13b	3.5	10673
TNFSF15	tumor necrosis factor (ligand) superfamily, member 15	3.2	9966
TOB1	transducer of ERBB2, 1	-4.2	10140
TOM1L1	target of myb1 (chicken)-like 1	-3.7	10040
TOP2A	topoisomerase (DNA) II alpha 170kDa	6.9	7153
TPM2	tropomyosin 2 (beta)	6.2	7169
TPM4	tropomyosin 4	3.6	7171
TPP1	tripeptidyl peptidase I	3.2	1200
TPST1	tyrosylprotein sulfotransferase 1	-6.1	8460
TRA2A	transformer 2 alpha homolog (Drosophila)	3.4	29896
TRAC	T cell receptor alpha constant	5.1	28755
TRAF3IP3	TRAF3 interacting protein 3	5.0	80342
TRAF5	TNF receptor-associated factor 5	4.8	7188
TRIM55	tripartite motif containing 55	-3.6	84675
TRNP1	TMF1-regulated nuclear protein 1	3.8	388610
TRPM8	transient receptor potential cation channel, subfamily M, member 8	-8.8	79054
TSLP	thymic stromal lymphopoietin	-3.2	85480
TSPAN12	tetraspanin 12	-5.2	23554
TSPAN6	tetraspanin 6	-3.4	7105
TTC36	tetratricopeptide repeat domain 36	-7.2	143941
TTC39C	tetratricopeptide repeat domain 39C	-4.2	125488
TTPA	tocopherol (alpha) transfer protein	-3.5	7274
TTR	transthyretin	-6.5	7276
TUBE1	tubulin, epsilon 1	-3.1	51175
TYROBP	TYRO protein tyrosine kinase binding protein	6.9	7305
UAP1	UDP-N-acteylglucosamine pyrophosphorylase 1	-3.3	6675

UBASH3B	ubiquitin associated and SH3 domain containing B	3.9	84959
UCP2	uncoupling protein 2 (mitochondrial, proton carrier)	7.6	7351
UGP2	UDP-glucose pyrophosphorylase 2	-4.3	7360
UGT2B15	UDP glucuronosyltransferase 2 family, polypeptide B15	-3.9	7366
UGT2B28	UDP glucuronosyltransferase 2 family, polypeptide B28	-4.9	54490
UGT2B4	UDP glucuronosyltransferase 2 family, polypeptide B4	-18.8	7363
UGT3A1	UDP glycosyltransferase 3 family, polypeptide A1	-7.7	133688
UPB1	ureidopropionase, beta	-5.4	51733
VCAN	versican	4.2	1462
VGLL3	vestigial like 3 (Drosophila)	3.4	389136
VIM	vimentin	4.5	7431
VMO1	vitelline membrane outer layer 1 homolog (chicken)	8.6	284013
VNN1	vanin 1	-4.4	8876
VNN3	vanin 3	-9.9	55350
VSIG4	V-set and immunoglobulin domain containing 4	10.0	11326
VTCN1	V-set domain containing T cell activation inhibitor 1	6.3	79679
VTN	vitronectin	-9.8	7448
WDR54	WD repeat domain 54	3.0	84058
WDR72	WD repeat domain 72	-5.2	256764
WFDC1	WAP four-disulfide core domain 1	5.2	58189
WIPF1	WAS/WASL interacting protein family, member 1	4.4	7456
WISP1	WNT1 inducible signaling pathway protein 1	8.4	8840
WNK3	WNK lysine deficient protein kinase 3	-4.0	65267
WNT3	wingless-type MMTV integration site family, member 3	-6.2	7473
WSB1	WD repeat and SOCS box containing 1	3.0	26118
XDH	xanthine dehydrogenase	-5.3	7498
XYLT1	xylosyltransferase I	3.1	64131
ZEB2	zinc finger E-box binding homeobox 2	3.1	9839
ZG16	zymogen granule protein 16 homolog (rat)	-3.6	653808
ZIC1	Zic family member 1	-5.4	7545
ZNF320	zinc finger protein 320	4.0	162967
ZNF385B	zinc finger protein 385B	-3.1	151126
ZNF83	zinc finger protein 83	3.4	55769
ZNF880	zinc finger protein 880	3.3	400713
ZWINT	ZW10 interactor	5.2	11130

Table S8. List of 111 miRNAs differentially expressed in patients with HBV-associated acute liver failure

miRNA Symbol (Affymetrix)	miRbase21	Fold Change
hp_hsa-mir-1826_st	primary transcript	1.7
hp_hsa-mir-194-2_x_st	primary transcript	-2.2
hp_hsa-mir-320c-1_st	primary transcript	-2.3
hsa-let-7i_st	let-7i-5p	3.5
hsa-miR-106a_st	miR-106a-5p	-1.6
hsa-miR-10a_st	miR-10a-5p	2.8
hsa-miR-122-star_st	miR-122-3p	-15.2
hsa-miR-1244_st	miR-1244	5.7
hsa-miR-125b-2-star_st	miR-125b-2-3p	-5.0
hsa-miR-1301_st	miR-1301-3p	4.2
hsa-miR-130a_st	miR-130a-3p	1.9
hsa-miR-132_st	miR-132-3p	3.3
hsa-miR-138_st	miR-138-1-3p	3.7
hsa-miR-138-1-star_st	miR-138-5p	-6.7
hsa-miR-143_st	miR-143-3p	1.8
hsa-miR-143-star_st	miR-143-5p	3.2
hsa-miR-146a_st	miR-146a-5p	7.8
hsa-miR-148a_st	miR-148a-3p	-9.0
hsa-miR-150_st	miR-150-5p	7.2
hsa-miR-154_st	miR-154-5p	4.4
hsa-miR-155_st	miR-155-5p	12.1
hsa-miR-15a_st	miR-15a-5p	2.0
hsa-miR-15b_st	miR-15b-5p	2.5
hsa-miR-17_st	miR-17-5p	-1.7
hsa-miR-181a-star_st	miR-181a-3p	3.7
hsa-miR-181b_st	miR-181b-5p	2.6
hsa-miR-181c_st	miR-181c-5p	4.3
hsa-miR-182_st	miR-182-5p	18.9
hsa-miR-183_st	miR-183-5p	1.9
hsa-miR-185_st	miR-185-5p	2.1
hsa-miR-18a-star_st	miR-18a-3p	1.7
hsa-miR-192_st	miR-192-3p	-10.1
hsa-miR-192-star_st	miR-192-5p	-24.8
hsa-miR-193a-5p_st	miR-193a-5p	-3.3
hsa-miR-193b_st	miR-193b-3p	-5.1
hsa-miR-193b-star_st	miR-193b-5p	-11.4
hsa-miR-194_st	miR-194-3p	-9.0
hsa-miR-194-star_st	miR-194-5p	-23.6
hsa-miR-1972_st	miR-1972	3.6
hsa-miR-1979_st	removed from the database	3.6
hsa-miR-199a-3p_st	miR-199a-3p	1.9
hsa-miR-199b-3p_st	miR-199b-3p	1.9
hsa-miR-200a_st	miR-200a-3p	4.7
hsa-miR-200a-star_st	miR-200a-5p	2.0
hsa-miR-200b_st	miR-200b-3p	7.2

hsa-miR-20a_st	miR-20a-5p	-2.2
hsa-miR-21_st	miR-210-3p	4.6
hsa-miR-210_st	miR-212-3p	-3.2
hsa-miR-212_st	miR-21-3p	7.5
hsa-miR-21-star_st	miR-21-5p	6.5
hsa-miR-221_st	miR-221-3p	2.8
hsa-miR-222_st	miR-222-3p	2.0
hsa-miR-223_st	miR-223-3p	7.8
hsa-miR-23a_st	miR-23a-3p	2.0
hsa-miR-23b-star_st	miR-23b-5p	-3.0
hsa-miR-24-2-star_st	miR-24-2-5p	8.7
hsa-miR-27b_st	miR-27b-3p	-2.8
hsa-miR-30a_st	miR-30a-5p	-2.2
hsa-miR-30b_st	miR-30b-3p	-2.4
hsa-miR-30b-star_st	miR-30b-5p	-4.5
hsa-miR-30c-1-star_st	miR-30c-1-3p	-2.5
hsa-miR-30e_st	miR-30e-5p	-2.5
hsa-miR-31_st	miR-31-5p	3.7
hsa-miR-3175_st	miR-3175	11.1
hsa-miR-3178_st	miR-3178	3.8
hsa-miR-330-3p_st	miR-330-3p	5.0
hsa-miR-342-3p_st	miR-342-3p	2.3
hsa-miR-342-5p_st	miR-342-5p	4.1
hsa-miR-345_st	miR-345-5p	-3.5
hsa-miR-34a-star_st	miR-34a-3p	1.9
hsa-miR-363_st	miR-363-3p	5.7
hsa-miR-370_st	miR-370-3p	6.4
hsa-miR-375_st	miR-375	-18.6
hsa-miR-376c_st	miR-376c-3p	5.7
hsa-miR-378_st	miR-378a-3p	-2.4
hsa-miR-378c_st	miR-378a-5p	-2.5
hsa-miR-378-star_st	miR-378c	-3.8
hsa-miR-381_st	miR-381-3p	3.3
hsa-miR-382_st	miR-382-5p	9.5
hsa-miR-409-3p_st	miR-409-3p	5.6
hsa-miR-409-5p_st	miR-409-5p	3.9
hsa-miR-421_st	miR-421	4.5
hsa-miR-422a_st	miR-422a	-2.3
hsa-miR-4269_st	miR-4269	4.7
hsa-miR-4298_st	miR-4298	-2.3
hsa-miR-4306_st	miR-4306	3.4
hsa-miR-431_st	miR-431-5p	4.8
hsa-miR-432_st	miR-432-5p	3.8
hsa-miR-433_st	miR-433-3p	4.4
hsa-miR-452_st	miR-452-5p	3.1
hsa-miR-455-3p_st	miR-455-3p	-2.6
hsa-miR-483-5p_st	miR-483-5p	-11.5
hsa-miR-485-5p_st	miR-485-5p	2.4
hsa-miR-487a_st	miR-487a-3p	2.8
hsa-miR-493_st	miR-493-3p	5.5
hsa-miR-495_st	miR-495-3p	1.7
hsa-miR-501-5p_st	miR-501-5p	2.9
hsa-miR-503_st	miR-503-5p	4.4

hsa-miR-542-5p_st	miR-542-5p	3.3
hsa-miR-543_st	miR-543	2.5
hsa-miR-574-3p_st	miR-574-3p	-4.8
hsa-miR-584_st	miR-584-5p	4.0
hsa-miR-625_st	miR-625-5p	5.5
hsa-miR-629_st	miR-629-5p	6.3
hsa-miR-652_st	miR-652-3p	2.9
hsa-miR-654-3p_st	miR-654-3p	3.0
hsa-miR-665_st	miR-665	3.8
hsa-miR-885-3p_st	miR-885-3p	-5.5
hsa-miR-885-5p_st	miR-885-5p	-43.5
hsa-miR-886-3p_st	removed from the database	14.4
hsa-miR-99b-star_st	miR-99b-3p	5.7

Table S9. Major microRNAs involved in B-cell development, regulation and response, their potential targets and the differential expression in livers of patients with HBV-associated acute liver failure, compared to normal livers

miRNA	Targets	Expression (Fold Change) in HBV-Associated Acute Liver Failure
miR-15a	BCL2 (11,44)	15a-5p **2.0**
miR-17-92 cluster	BIM, PTEN (12, 16, 18, 28, 35, 41)	17-5p **-1.7** 20a-5p **-2.2** 18a-3p **1.7**
miR-21	PDCD4 (9)	21-5p **4.6** 21-3p **6.5**
miR-23b	BLIMP1 (37, 38)	23b-5p **-3.0**
miR-24	BIM, CASP9 (22)	24-2-5p **8.7**
miR-30 family	AID, BLIMP1 (39, 43, 46), BCL6 (14)	30a-5p **-2.2** 30b-5p **-2.4** 30b-3p **-4.5** 30c-1-3p **-2.5** 30e-5p **-2.5**
miR-34a	FOXP1 (26)	34a-3p **1.9**
miR-125b	ARID3a (25)	125b-2-3p **-5.0**
miR-146a	FAS, FADD, IRAK1, IRAK2, IRF5, TRAF6 (1, 7, 10, 20)	146a-5p **7.8**
miR-150	C-MYB (19, 40, 45)	150-5p **7.2**
miR-155	AID, C-MAF, SHP1, SPI1 (2, 4, 6, 8, 13, 17, 23, 24, 27, 29, 30, 32-34, 36, 37, 42)	155-5p **12.1**
miR-181a	BIM, DUSP5, DUSP6, PTPN22, SHP2 (3, 15, 21)	181a-3p **3.7**
miR-181b	AID, BCL2 (5, 31, 47)	181b-5p **2.6**

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Table S10. Results of phage-display library screening for antigen- specific Fab clones after three cycles of panning

Patient/Chimpanzee	Antibody Library	Antigen	% Positive Clones (from 96 Clones Screened)
Patient 31	IgM	BSA	0
		31 HBsAg	0
		31 HBcAg	99
	IgG	BSA	0
		31 HBsAg	0
		31 HBcAg	92
Patient 32	IgM	BSA	0
		32 HBsAg	0
		32 HBcAg	93
	IgG	BSA	0
		32 HBsAg	0
		32 HBcAg	99
Patient 219	IgM	BSA	0
		219 HBsAg	0
		219 HBcAg	96
	IgG	BSA	0
		219 HBsAg	0
		219 HBcAg	92
Patient 241	IgM	BSA	0
		241 HBsAg	0
		241 HBcAg	98
	IgG	BSA	0
		241 HBsAg	0
		241 HBcAg	95
Chimpanzee 1627	IgG	BSA	0
		Ayw HBsAg	0
		Ayw HBcAg	98
Chimpanzee 5835	IgG	BSA	0
		Ayw HBsAg	0
		Ayw HBcAg	100

Table S11. Titer of HBcAg-specific IgM and IgG extracted from the liver of patients with HBV-associated acute liver failure (ALF) and from one healthy liver donor

HBcAg	Healthy Donor		ALF Patients			
	2PF		219		241	
	IgM	IgG	IgM	IgG	IgM	IgG
ayw	0	0	1:2430	1:810	1:1260	1:1260
219	0	0	1:2430	1:2430	1:3777	1:3777
241	0	0	1:2430	1:2430	1:3777	1:11,330

Table S12. Identical V(D)J sequences appearing in both IgG and IgM samples in patients with acute liver failure

Patient	Group ID	Sequence ID		V(D)J Sequences
241	1	241IgM_B1 (2)*	241IgG_F7 (1)	LEESGGGLVKPGGSLRLSCAASGFTFSNAWMSWVRQAPGKGLEWVGR IKSKTDGGTTDYAAPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYY CTTDLVVPAAMYSYYYYYGMDVWGQGTTVTV
	2	241IgM_B4 (1)	241IgG_A12 (2)	LEQSGGGVVQPGRSLRLSCAASGFTFSSYAMHWVRQAPGKGLEWVAV ISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCA RDLLPSLGYSSLLGYWGQGTLVTVS
	3	241IgM_B8 (2)	241IgG_A7 (2)	LEESGGGVVQPGRSLRLSCAASGFTFSSYAMHWVRQAPGKGLEWVAV ISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCA RDLLPDIAVAGTRGPGYWGQGTLVTVS
	4	241IgM_B11 (1)	241IgG_F2 (6)	LEESGGGVVQPGRSLRLSCAASGFTFSSYAMHWVRQAPGKGLEWVAV ISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCA RALLPGIAAAGSSELGYWGQGTLVTVS
	5	241IgM_D6 (1)	241IgG_H2 (6)	LEQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGI INPSGGSTSYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCA RDWGFYSSGYYYGMDVWGQGTTVTVS
	6	241IgM_E2 (3)	241IgG_F6 (3)	LEQSGGGVVQPGRSLRLSCAASGFTFSSYAMHWVRQAPGKGLEWVAV ISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCA RDLLPSITMIPSLGYWGQGTLVTVS
	7	241IgM_F10 (10)	241IgG_H6 (14)	LEQSGGGLVKPGGSLRLSCAASGFTFSNAWMSWVRQAPGKGLEWVGR IKSKTDGGTTDYAAPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYY CTTDLREVDSYGYGYYYYYGMDVWGQGTTVTV
31	8	31IgM_B10 (2)	31IgG_C10 (1)	LEESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSY ISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCA RDVYYDSSGYYYGLDYWGQGTLVTVS
	9	31IgM_D5 (1)	31IgG_D7 (6)	LEQSGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCA KEGVAVAGFTPFDYWGQGTLVTVS
	10	31IgM_F7 (1)	31IgG_D3 (1)	LEQSGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCA KEFVDTAMVTPLDYWGQGTLVTVSS
	11	31IgM_F10 (3)	31IgG_F5 (2)	LEQSGAEVKKPGASVKVSCKASGYTFTSYAMHWVRQAPGQRLEWMGW INAGNGNTKYSQKFQGRVTITRDTSASTAYMELSSLRSEDTAVYYCA RAMHLDDYYYYGMDVWGQGTTVTVS
	12	31IgM_G9 (17)	31IgG_C11 (6)	LEQSGAEVKKPGASVKVSCKASGYTFTSYGISWVRQAPGQGLEWMGW ISAYNGNTNYAQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCA RGLYYDYVWGSYRLDYWGQGTLVTVS
219	13	219IgM_A9 (66)	219IgG_D6 (21)	LEESGGGLVQPGGSLRLSCAVSGFTFSSYAMSWVRQAPGKGLEWVSG ISDSGGNTYYADSVKGRFTLSRDNSKNTLYLQMNSLRADDTAVYYCA KDLLWEPRGYFDYWGQGTLVTVS
	14	219IgM_G10 (4)	219IgG_G3 (1)	LEESGGGLVQPGGSLRLTCAVSGFTFSSYAMSWVRQAPGKGLEWVSG ISDSGDNTYYADSVKGRFTLSRDNSKNTLYLQMNSLRADDTAVYYCA KDLLWEPRGYFDYWGQGTLVTVS
32	15	32IgM_A6 (80)	32IgG_E1 (82)	LEESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCA KYPWGETNGAFDIWGQGTMVTVS
31/32	16	32IgM_C4 (1)	31IgG_H11 (3)	LEQSGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCA KFPWDTAMGPFDYWGQGTLVTVSSAS

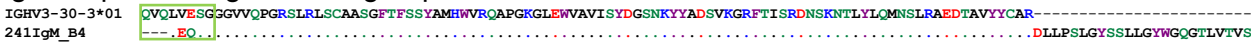
*Numbers in parenthesis represent the repeat number (prevalence) of the sequence. The HCDR3 (VDJ junction) are shown in blue color.

Table S13. Sequence alignment of IgG and IgM antibodies in patients with acute liver failure. The group IDs are the same as those presented in Table S12

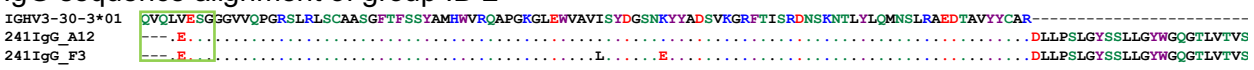
IgM sequence alignment of group ID 1

IgG sequence alignment of group ID 1

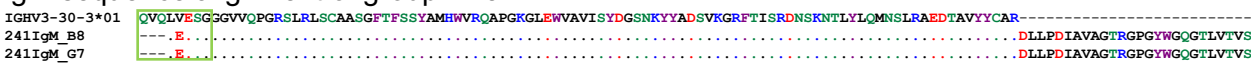
IgM sequence alignment of group ID 2



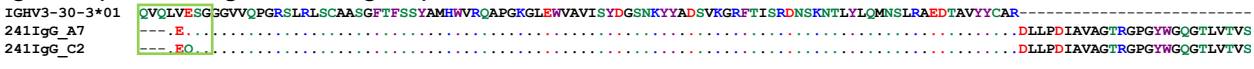
IgG sequence alignment of group ID 2



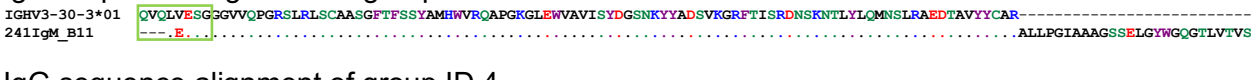
IgM sequence alignment of group ID 3



IgG sequence alignment of group ID 3



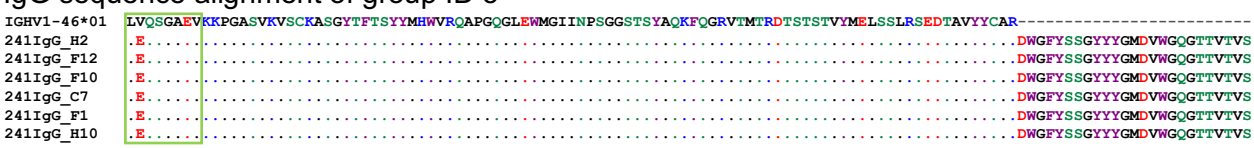
IgM sequence alignment of group ID 4



IgG sequence alignment of group ID 4

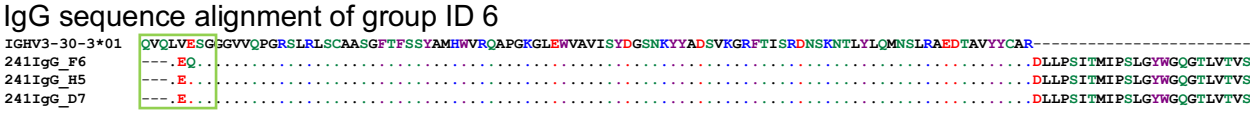
IgM sequence alignment of group ID 5

IgG sequence alignment of group ID 5

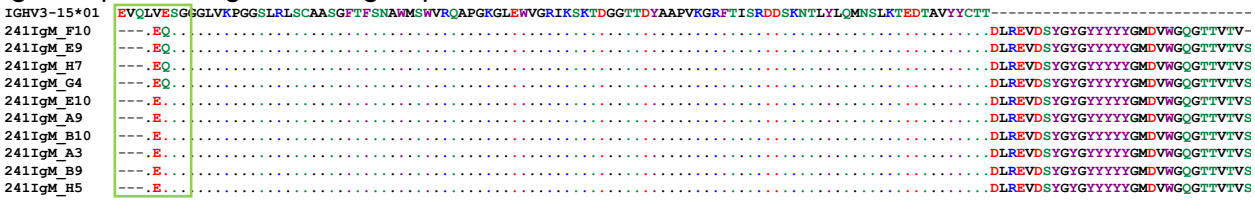


IgM sequence alignment of group ID 6

IgG sequence alignment of group ID 6

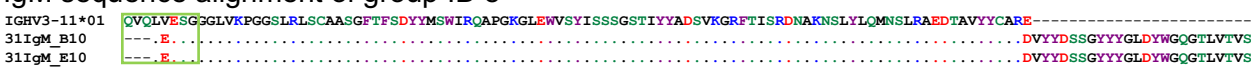


IgM sequence alignment of group ID 7



IgG sequence alignment of group ID 7

IgM sequence alignment of group ID 8



IgG sequence alignment of group ID 8

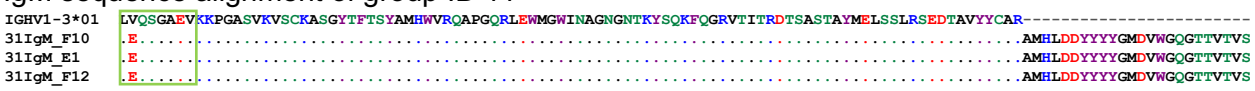
IgM sequence alignment of group ID 9

IgG sequence alignment of group ID 9

IgM sequence alignment of group ID 10

IgG sequence alignment of group ID 10

IgM sequence alignment of group ID 11

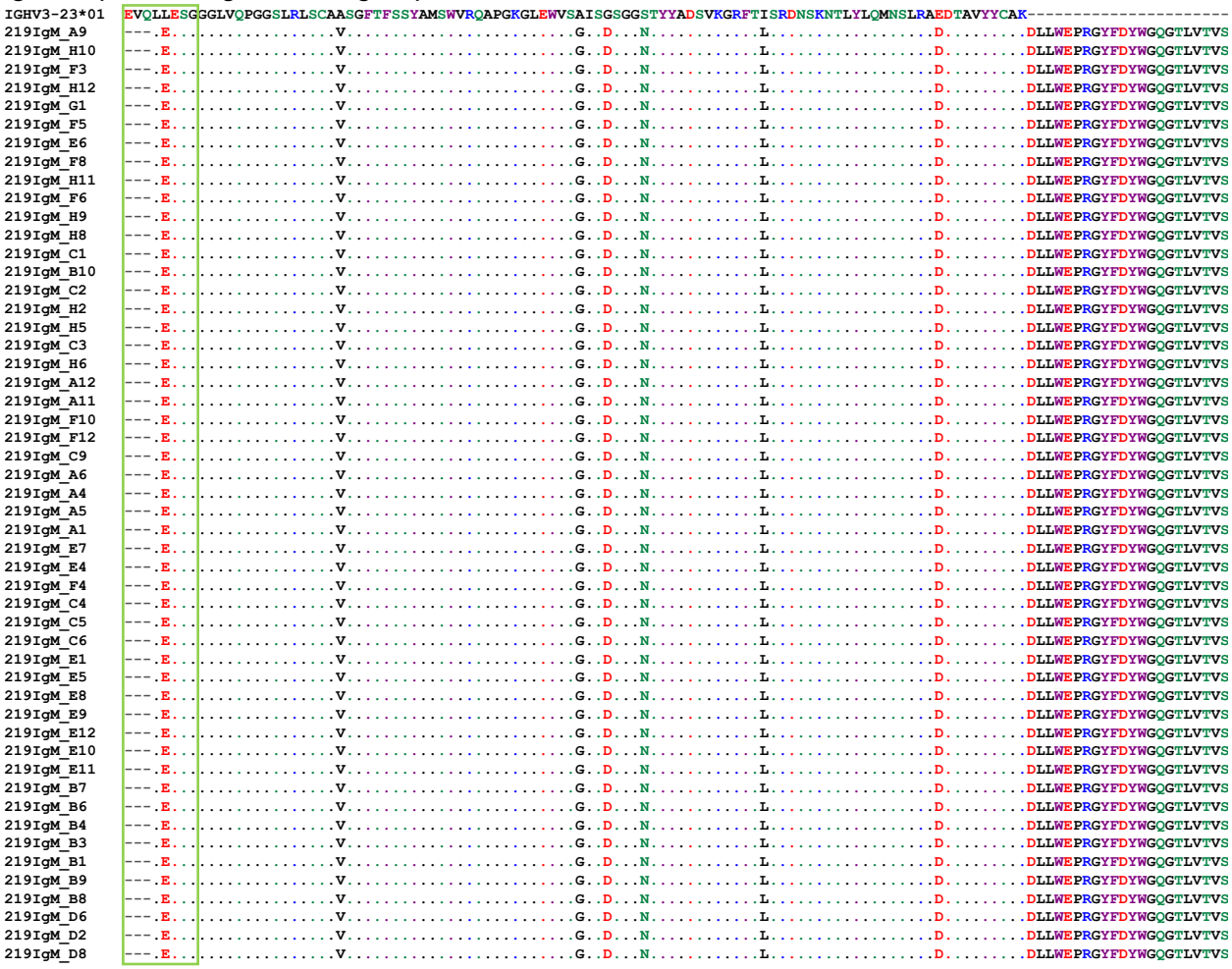


IgG sequence alignment of group ID 11

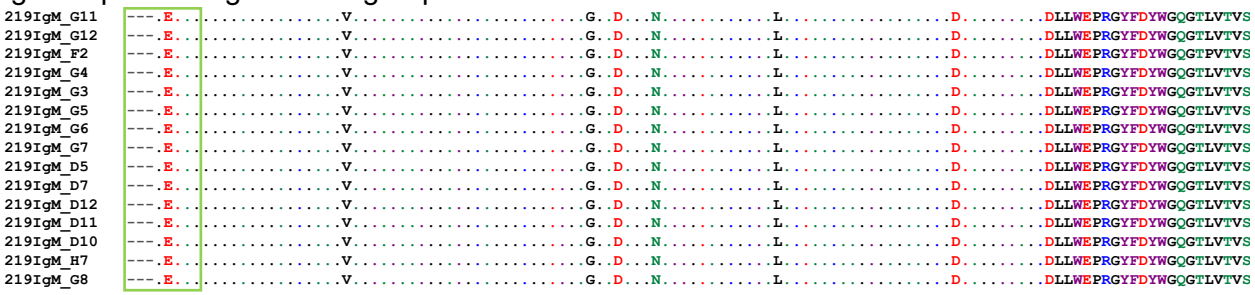
IgM sequence alignment of group ID 12

IgG sequence alignment of group ID 12

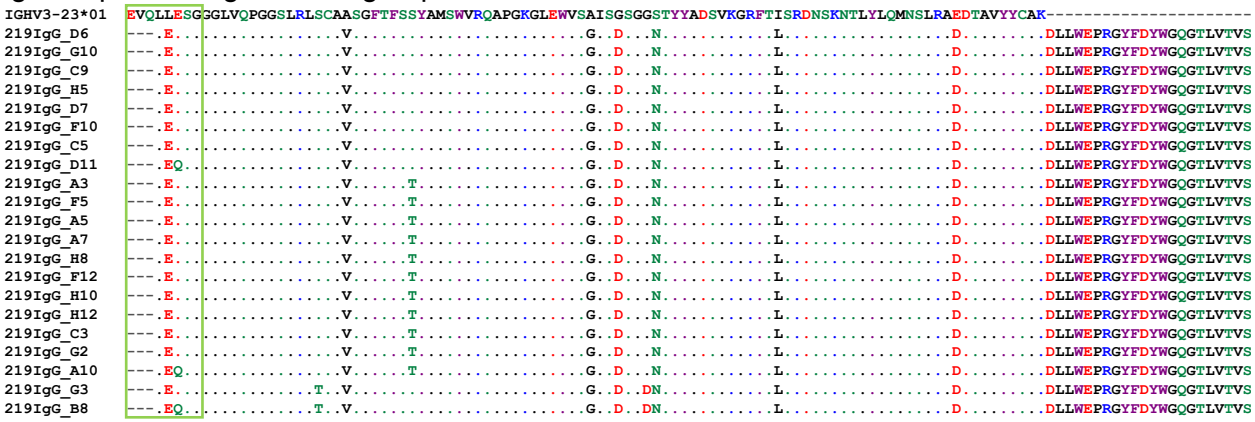
IgM sequence alignment of group ID 13



IgM sequence alignment of group ID 13 continued

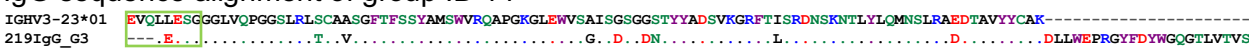


IgG sequence alignment of group ID 13

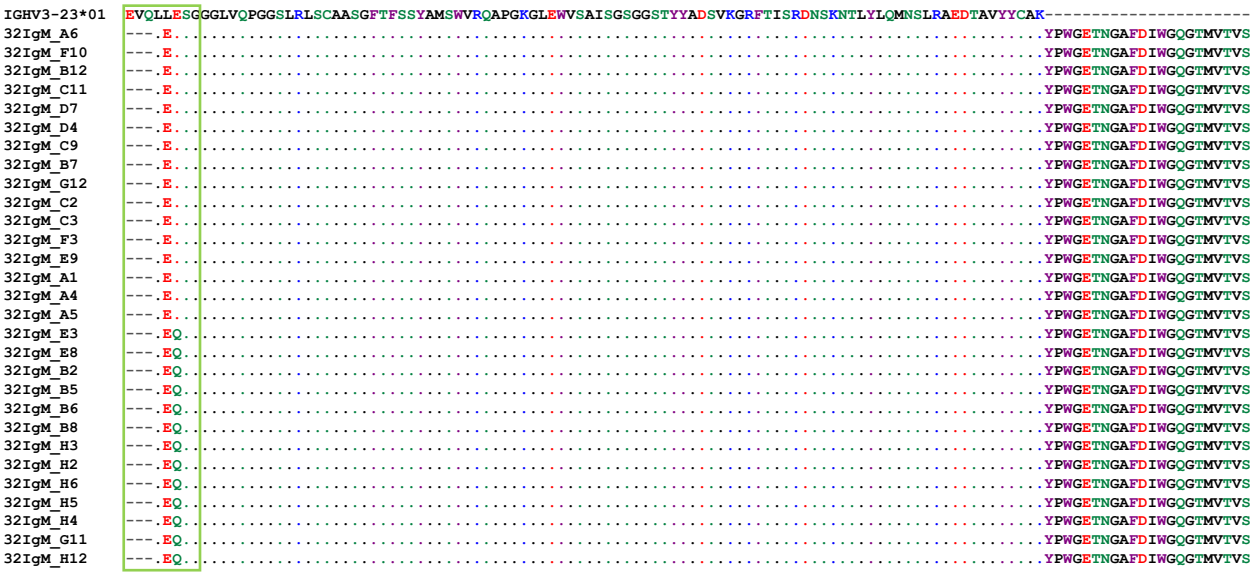


IgM sequence alignment of group ID 14

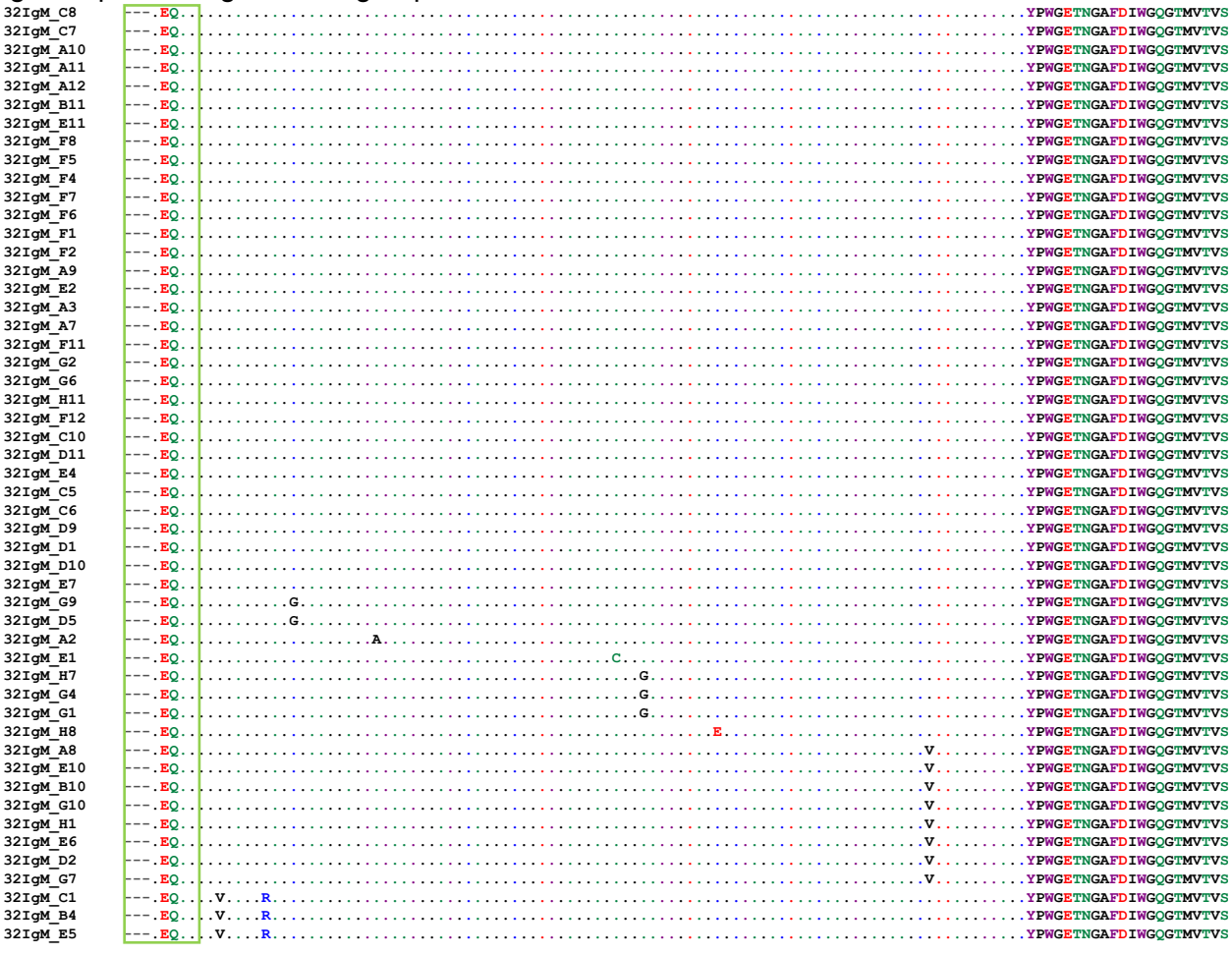
IgG sequence alignment of group ID 14



IgM sequence alignment of group ID 15



IgM sequence alignment of group ID 15 continued



IgG sequence alignment of group ID 15

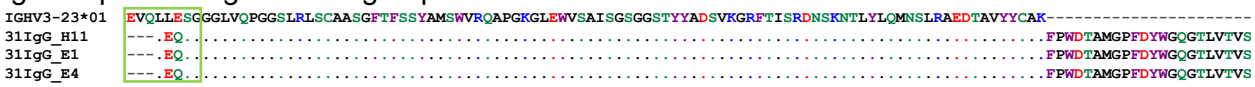
```
IGHV3-23*01  EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK----------------------
32IgG_E1     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_A8     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_A9     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_A6     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_A5     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_B9     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_B8     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_B3     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_B5     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_B4     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_H9     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_D12    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_G5     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_A11    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_F6     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_H1     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_H5     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_H7     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_E10    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_C9     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_C1     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_C7     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_D4     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_D6     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_D3     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_H12    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_H11    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_G11    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_E9     ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
```

IgG sequence alignment of group ID 15 continued

```
241IgG_G11   ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_G10   ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_G12   ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_E8    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_E4    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_B1    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_B2    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_B3    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_B4    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_B8    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_B9    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_C10   ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_E11   ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_G9    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_G6    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_G5    ---.E.....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_G2    ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_G3    ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_E12   ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_B7    ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_B12   ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_E2     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_G12    ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_G10    ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_E11    ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_F10    ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_H10    ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_D1     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_D7     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_D9     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_C6     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_C3     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_A7     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_F8     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_G9     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_G8     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_G1     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_G6     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_G4     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_B1     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_F1     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_F5     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_A1     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_E4     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_A4     ---.EQ....................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_C8     ---.E.....................................A..............................................YPWGETNGAFDIWGQGTMVTVS
32IgG_B11    ---.EQ...V................................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_D2     ---.EQ....................................................................G...............YPWGETNGAFDIWGQGTMVTVS
32IgG_E3     ---.E.....V....R..........................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_E3    ---.E.....V....R..........................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_B12    ---.E.....K..R......T.....................................................................YPWGETNGAFDIWGQGTMVTVS
241IgG_E9    ---.E.....K..R......T.....................................................................YPWGETNGAFDIWGQGTMVTVS
32IgG_H8     ---.E.....................................VG..............R.....................YPWGETNGAFDIWGQGTMVTVS
```

IgM sequence alignment of group ID 16

IgG sequence alignment of group ID 16



The first 8 amino acids bracketed by green rectangle belong to the primer sequence. The chemical characteristics of the color-coded amino acids are: **HKR**, polar positive charge; **DE**, polar negative charge; **CNQST**, polar neutral; AGILMPV, non-polar neutral; **FWY**, nonpolar aromatic neutral.

Table S14. Property and prevalence of high-affinity germline anti-core clones in the intrahepatic IgM and IgG repertoire assessed by next generation sequencing (NGS)

Property of germline anti-core antibody clones[1]			Prevalence of the specific clones in unselected IgM and IgG libraries revealed by NGS[3]									
Clone[2]	Origin	Gene Usage	31[4]		241		32		219		37	
			IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG
F10	241-IgM/IgG	V3-15,D5-18,J6	0	0	$2.5x10^{-4}$ ($1.9x10^{-4}$)	$1.1x10^{-3}$ ($1.6x10^{-3}$)	0	0	0	$2.4x10^{-6}$ ($7x10^{-7}$)	0	0
G3	32-IgM/IgG	V3-23,D3-16,J3	0	0	0	0	$2.5x10^{-5}$ ($4x10^{-5}$)	$1.9x10^{-4}$ ($2.4x10^{-4}$)	0	$2.4x10^{-6}$ ($5.3x10^{-7}$)	0	$5.5x10^{-6}$ ($7x10^{-6}$)
C7	219-IgG	V3-49,D2-8,J5	0	0	0	0	0	0	0	$1.5x10^{-5}$ ($1.3x10^{-5}$)	0	0
F4/B8	31-IgG	V3-23,D1-1,J3	$2.4x10^{-6}$ ($3.1x10^{-6}$)	$1x10^{-5}$ ($6.9x10^{-6}$)	0	0	0	0	0	0	0	0
B7	31-IgM/IgG	V1-18,D3-16,J4	$7.3x10^{-6}$ ($1.1x10^{-5}$)	$5.2x10^{-6}$ ($1.8x10^{-6}$)	0	0	0	0	0	0	0	0

1. Antibody clones were identified by phage display library from the liver of ALF patients and panned against HBcAg.
2. Clones F4 and B8 were combined because they use the same genes with 0-2 mutations.
3. The prevalence of the high-affinity anti-core clones were assessed by two methods: (I) based on unique duplicate sequences as shown by numbers and (II) based on sequencing reads as shown by numbers in parentheses.
4. The IgM and IgG libraries were made from the liver of ALF-patient 31, 241, 32 and 219 as well as from a healthy liver donor 37 that was, negative for serologic markers of HBV infection.

Table S15. Number of somatic mutations within the variable heavy chain (V_H) gene and binding affinity to hepatitis B core antigen (HBcAg) measured by surface plasmon resonance of selected Fabs recovered from the livers of patients with HBV-associated acute liver failure (ALF) and chimpanzees with acute hepatitis B

Disease	Fab	Origin	No. of Mutations in V_H Gene[1]	Gene Usage	Reads	HBcAg Antigen[2]	*Binding Kinetics* k_{off} (sec^{-1})	k_{on} ($nM^{-1}sec^{-1}$)	K_d (nM)
HBV ALF	F10	241-IgM/IgG	0	V3-15,D5-18,J6	14/70	31	2.30E-05	8.55E-08	269
						32	6.22E-03	4.01E-04	15.5
						241	1.76E-03	2.46E-04	7.14
						219	2.64E-02	5.71E-04	46.2
						ayw	9.44E-05	4.56E-07	207
	G3	32-IgM/IgG	0	V3-23,D3-16,J3	3/59	31	1.33E-05	7.92E-05	0.168
						32	2.60E-05	1.06E-04	0.246
						241	1.63E-04	1.12E-04	1.45
						219	8.21E-05	1.46E-04	0.562
						ayw	4.54E-05	1.63E-04	0.278
	F4	31-IgG	0	V3-23,D1-1,J3	11	31	1.87E-04	1.40E-04	1.34
						32	2.15E-03	1.55E-04	13.9
						241	5.48E-03	1.58E-04	34.6
						219	1.41E-02	2.01E-04	70.1
						ayw	1.40E-02	2.46E-04	57
	B7	31-IgM/IgG	0	V1-18,D3-16,J4	18/7	31	1.41E-04	3.32E-05	4.25
						32	1.08E-04	5.93E-06	18.2
						241	3.17E-04	1.07E-05	29.7
						219	6.23E-05	2.78E-05	2.24
						ayw	1.68E-05	5.62E-05	0.299
	C7	219-IgG	0	V3-49,D2-8,J5	23	31	5.76E-05	1.39E-04	0.415
						32	5.23E-04	1.97E-04	2.65
						241	2.15E-05	1.54E-04	0.14
						219	2.60E-05	1.86E-04	0.14
						ayw	1.42E-05	3.06E-04	0.0464
	B8	31-IgG	2	V3-23, D1-1, J3	3	31	2.21E-04	1.35E-04	1.64
						32	1.19E-03	1.10E-04	10.8
						241	6.33E-03	1.27E-04	49.7
						219	8.23E-03	1.44E-04	57.3
						ayw	7.90E-03	1.31E-04	60.2
	B4	32-IgM	3	V3-23, D3-16, J3	82	31	1.10E-05	1.04E-04	0.106
						32	2.48E-05	9.61E-05	0.258
						241	NB[3]	NB	NB
						219	4.57E-05	1.14E-04	0.402
						ayw	2.74E-05	1.70E-04	0.161
	E3	219-IgG	8	V3-23, D3-16, J4	5	31	2.05E-05	1.60E-04	0.128
						32	6.47E-05	1.07E-04	0.604
						241	3.52E-05	1.67E-04	0.211
						219	2.05E-04	1.74E-04	1.18
						ayw	1.36E-04	2.20E-04	0.619
	G10	219-IgG/IgM	11	V3-23, D6-13, J4	21/93	31	9.19E-04	2.87E-04	3.2
						32	1.04E-03	6.80E-04	1.53
						241	3.16E-03	2.59E-04	12.2
						219	3.38E-03	4.36E-04	7.75
						ayw	1.89E-03	4.18E-06	452
	D5	219-IgG	20	V1-46, D5-18, J3	1	31	4.39E-05	1.87E-07	235
						32	1.13E-03	3.91E-05	28.9
						241	9.71E-05	2.09E-07	465
						219	3.65E-04	4.24E-05	8.6
						ayw	3.11E-04	2.21E-05	14.1
	C2	31-IgG	27	V3-23, D3-22, J4	6	31	5.07E-03	1.88E-04	26.9
						32	NB	NB	NB
						241	1.78E-02	1.78E-04	100
						219	NB	NB	NB
						ayw	NB	NB	NB

Acute Hepatitis B	**D10**	CH1627-IgG	6	V6-1,D6-19,J3	69	31	NB[3]	NB	NB
						32	5.42E-04	1.99E-06	273
						241	NB	NB	NB
						219	NB	NB	NB
						ayw	6.01E-3	4.89E-04	12.3
	F8	CH1627-IgG	19	V3-74,D2-2,J4	14	31	9.80E-4	1.55E-06	631
						32	3.91E-03	4.36E-04	8.97
						241	NB	NB	NB
						219	4.46E-04	3.35E-04	1.33
						ayw	2.08E-3	3.85E-4	5.40
	A1	CH5835-IgG	11	V3-74,D4-11,J4	12	31	NB	NB	NB
						32	1.08E-01	1.31E-04	822
						241	NB	NB	NB
						219	>1.00E-01	NB	25.91[4]
						ayw	5.31E-04	1.21E-03	0.439
	B9	CH5835-IgG	9	V3-74,D5-12,J4	41	31	NB	NB	NB
						32	1.52E-01	1.79E-04	847
						241	NB	NB	NB
						219	1.45E-04	2.11E-07	687
						ayw	4.43E-04	1.00E-03	0.443

1. Number of nucleotide substitutions in VH gene.
2. Hepatitis B core protein was derived from patient 31, 32, 241 and 219 with ALF or wild-type HBV (ayw) (8)
3. No binding detectable
4. K_d was determined by isotherm analysis using steady-state signal as a function of analyte concentration.