

**A**

```

-----_CDRH1-----_CDRH2-----
HV6-1*01  QVQLQQSGPGLVKPQSQTLSLTCALSGDSVSSNSAAWNWIRQSPSRGLEWLGRTYYRSKWYNDYAVSVKSRITINPDTSKNFSQLQNSVTPEDTAVYYCAR
31.g.01  .....V...T...D...R...Y.F...T...M...D...F...
54.f.01  .....R...V...H...S...P...T...A...E.I...Y...V...
56.a.09  .....V...T...R...T...T...T...T...MK...

-----_CDRH_1-----_CDRH_2-----
HV1-18*01  QVQLVQSGAEVKKPGASVKVCSKASGYTFYTSYGISWVRQAPGGQLEWGMWISAYNGNTNYAQKLGQRVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR
01.k.01  H.H.....QES.....S.S.H.....H...L.F...L...D...
31.b.09  .....S.S.....F...

-----_CDRH_1-----_CDRH_2-----
HV1-18*01  QVQLVQSGAEVKKPGASVKVCSKASGYTFYTSYGISWVRQAPGGQLEWGMWISAYNGNTNYAQKLGQRVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR
16.g.07  ...A..EN.L.....T...RF.M.....G.T.D.K..RSF...L.L...G.....I...V...
54.a.84  .....P...R...T...SR.....P...A...T.D.H..R.F...VS.EA..A.V...
16.a.26  .....P...S.SR.....L...G.T...F...S...
54.a.39  ..H.....V.....A...T...F...FKD..VS...T...G..Y...

-----_CDRH_1-----_CDRH_2-----
HV3-23     EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK
31.a.83    .....E..V.....D...L.....N..A...T...QT...D...T...

```

**B****HV6-1+HD3-3**

```

-----VH6-1-----VHD3-3*01-----VHJ4-----
C A R I T I F G V V I I Y F D Y W
TGTGCGAGAGA GGATACGATTTTGACTGGTATATAAAG AGACCTTGACTACTGG
C A R D S F M I F G I V F V D Y W
HV6-1+HD3-3.1.SRP015957  TGTGCGAAGA gagtcaccTATGATTTTGGATagatcatgaca gttGACTACTGG

```

**HV1-18+HD3-9**

```

-----VH1-18-----VHD3-9*01-----VHJ4-----
C A R Y Y D I L T G Y Y N Y F D Y W
TGTGCGAGAGA GGATACGATTTTGACTGGTATATAAAG AGACCTTGACTACTGG
C A R D R R D I L T G P R L D Y W
HV1-18+HD3-9.1.SRP015957  TGTACGAGA gacagaggaCATATTTTGACTGGTggcgagac TGACTACTGG

```

```

-----VH1-18-----VHD3-9*01-----VHJ4-----
C A R Y Y D I L T G Y Y N Y F D Y W
TGTGCGAGAGA GGATACGATTTTGACTGGTATATAAAG AGACCTTGACTACTGG
C A R D R R D I L T G P R L D Y W
HV1-18+HD3-9.2.SRP015957  TGTGCGAGA gatagggcCGACATTTTGACTGGTcccgatgg GACTACTGG

```

```

-----VH1-18-----VHD3-9*01-----VHJ4-----
C A R Y Y D I L T G Y Y N Y F D Y W
TGTGCGAGAGA GGATACGATTTTGACTGGTATATAAAG AGACCTTGACTACTGG
C A R S R R D I L T G Y N D D Y W
HV1-18+HD3-9.3.SRP015957  TGTGCGAGg tctgggcCGATATTTTGACTGGTtataacgac GACTACTGG

```

```

-----VH1-18-----VHD3-9*01-----VHJ4-----
C A R Y Y D I L T G Y Y N Y F D Y W
TGTGCGAGAGA GGATACGATTTTGACTGGTATATAAAG AGACCTTGACTACTGG
C A R D R G V I L T G S F F G D Y W
HV1-18+HD3-9.4.SRP047462  TGTGCGAGA gacgggggtgCATTTTGACTGGTtctcccgc GACTACTGG

```

**HV1-18 (QxxV)**

```

-----VH1-18-----VHD1R1-----VHJ4-----
C A R G G P R A Q G A P Y F D Y W
TGTGCGAGAGA GGATACGATTTTGACTGGTATATAAAG AGACCTTGACTACTGG
C A R D G A Q S F V V A R Q V W Q S D S W
HV1-18Qxxv.1.SRP015957  TGTGCGAGA gatgagcACAGGGtttggctggctcaagttggcaag TGACTCTGG

```

```

-----VH1-18-----VHD6-19*01-----VHJ5-----
C A R G I A V A G N W F D P W
TGTGCGAGAGA GGGTATACAGTGGCTGTGAC AGACCTTGACTACTGG
C A R D K I Q C W V A V A G T G N W F D P W
HV1-18Qxxv.2.SRP015957  TGTGCGAGA gataagatcaggggtgggTAGCAGTgactggaacggg CTGGTCCACCCCTGG

```

```

-----VH1-18-----VHD6-19*01-----VHJ5-----
C A R G I A V A G N W F D P W
TGTGCGAGAGA GGGTATACAGTGGCTGTGAC AGACCTTGACTACTGG
C A R D K V Q S W V A V A G T G N W F D P W
HV1-18Qxxv.3.SRP015957  TGTGCGAGA gataaagtccaggggtgggTAGCgctggctgctacggg CTGGTCCACCCCTGG

```

**C****HV1-18+HD3-9**

```

-----VH1-18-----VHD3-9*01-----VHJ3-----
C A R Y Y D I L T G Y Y N D A F D I W
TGTGCGAGAGA GGATACGATTTTGACTGGTATATAAAG AGACCTTGACTACTGG
C A R E R Y D I L T G D A F D I W
HV1-18+HD3-9.1.SRP026397  TGTGCGAGA gaaagTACGATATTTTGACTGG TGATCTTTGATATCTGG

```

```

-----VH1-18-----VHD3-9*01-----VHJ4-----
C A R Y Y D I L T G Y Y N Y F D Y W
TGTGCGAGAGA GGATACGATTTTGACTGGTATATAAAG AGACCTTGACTACTGG
C A R D R G D I L T G P S L D Y W
HV1-18+HD3-9.2.SRP073039  TGTGCGAGA gatcgtggCGATATTTTGACTGGgccatcg cTGACTACTGG

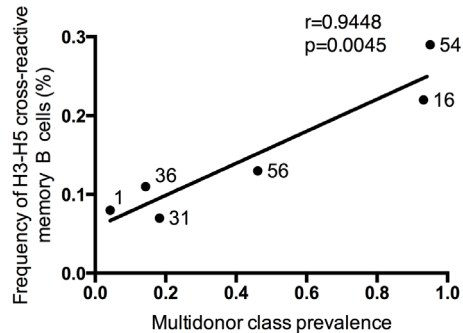
```

**HV1-18 (QxxV)**

```

-----VH1-18-----VHD4-4*01R-----VHJ6-----
C A R V V T V V Y Y Y Y Y G M D V W
TGTGCGAGAGA GGATACGATTTTGACTGGTATATAAAG AGACCTTGACTACTGG
C A R D K V Q G I V T V V H K A L D V W
HV1-18Qxxv.1.SRP026397  TGTGCGAGA gacaaggttcaggaattgACTGTAGTtcataaagct cTGACCTTGG

```

**D**

**Figure S6. Multidonor class sequences: somatic hypermutations, NGS-junction analysis, and transcript frequencies, related to Figures 2-7. (A)** Amino sequence alignment of V-gene region with the corresponding germline genes for all structurally characterized antibodies. **(B)** Consensus sequences containing multidonor class signatures derived from NGS data (SRP015957 and SRP047462) from influenza-vaccinated donors. **(C)** Consensus sequences containing multidonor class signatures derived from NGS data (SRP026397 and SRP073039) from normal donors. Each sequence label contains a unique index number along with the multidonor signature class name and SRP number the sequence derives from. Germline gene-encoded nucleotide and amino acid residues are shown in black with the corresponding junctions colored in light blue. Amino acids and nucleotides subject to somatic hypermutation are colored red. Nucleotides removed by exonuclease trimming are crossed out. All N, P additions occurring at the junctions are from JOINSOLVER (<http://joinsolver.niaid.nih.gov/>). We note that for the single sequence belonging to the HV6-1+HD3-3 class, we used the HD3-3\*01 germline D sequence instead of the HD3/OR15 germline D sequence even though the latter sequence matches better (by one nucleotide). **(D)** The percent frequency of multidonor class antibodies in each donor is highly correlated with the frequency of H3-H5 cross-reactive memory B cells. Correlation method: Pearson with a two-tailed test (n=6).