

Table S1: List of host proteins reactive to influenza bNAbs in ProtoArrays

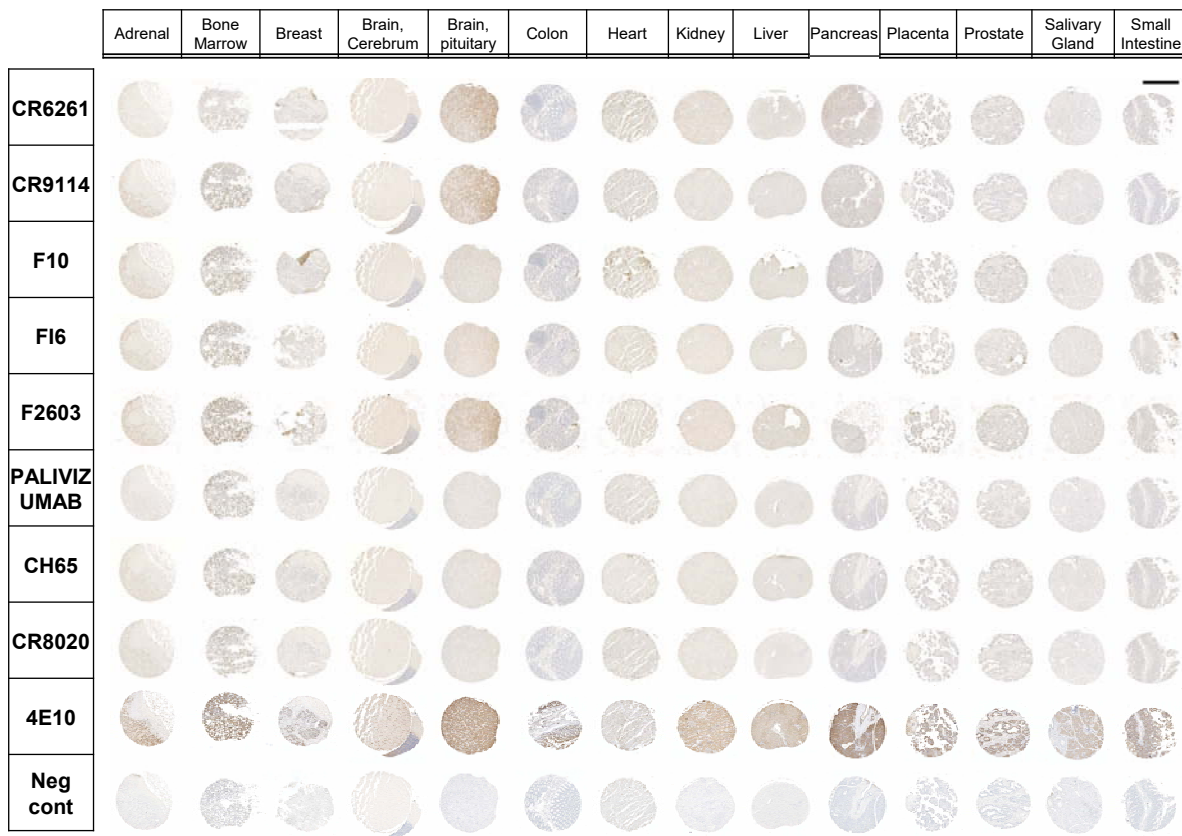
Protein	
1	N-acylaminoacyl-peptide hydrolase (APEH)
2	Enhancer of mRNA decapping 3 homolog (<i>S. cerevisiae</i>) (EDC3)
3	Serine/threonine/tyrosine interacting protein (STYX)
4	Tripartite motif-containing 21 (TRIM21)
5	Signal transducer and activator of transcription 4 (STAT4)
6	Mitogen-activated protein kinase 6 (MAPK6)
7	JO-1
8	Thyroglobulin

Table S2: Signal binding ratio of representative bNAbs relative to control 151K signal in IgG depleted human sera in ProtoArray.

PROTEIN	C6261	C8020	F10
STAT4	681.96	222.41	2.05
APEH	503.80	1.64	1.41
EDC3	221.14	2.41	1.22
TRIM21	2.37	2.37	2.19
BIRC8	4.66	122.51	1.65
STYX	2.70	182.46	1.63

Table S3: Competition of host proteins with Influenza HA binding to bNAbs

	C6261	CR8020	C9114	F10	FI6	C179	CH65
	%H1	%H3	%H1	%H1	%H1	%H1	%H1
APEH	100	100	99.3	100	100	99.7	98.9
TRIM21	100	99.2	100	100	100	96.3	100
EDC3	23.1	99.3	93.3	99.8	92.9	97.8	100
STYX	100	96.7	95.8	100	100	99.9	100
STAT4	100	100	98.1	100	91.6	89.6	90
MAPK6	100	93.9	97.2	100	100	92.6	94.5
JO-1	95.4	94.5	87.3	88.7	96.2	92.2	98.5
Thyroglobulin	99.2	100	93	100	99.6	94.4	94.9



Supplementary figure 1. Representative binding images of each bNAb to normal human tissues. Scales indicates 1 mm.

10 20 30 40 50 60
|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
 MATDWLGSIVSINCGDSLGVYQGRVSAVDQVSQTISLTRPFHNGVKCLVPEVTFRAGDIT

70 80 90 100 110 120
|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
 ELKILEIPGPGDNQHFGLHQTELGPSGAGCQVGINQNGTGKFKVPASSSSAPQNIPIKR

130 140 150 160 170 180
|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
 TDVKSQDVAVSPQQQCSKSYVDRHMELSQSFSFRRHNSWSSSRHPNQATPKKSGLK

190 200 210 220 230 240
|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
 NGQMKNKDDECFGDDIEEIPDIDFDIEGNLALFDKAAVFEEIDTYERRSGTRSRGIPNER

250 260 270 280 290 300
|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
 PTRYRHDENIIESEPIVYRRIIVPHNVSKEFCDSGLVVPSSISYELHKKLLSVAEKHGLT

310 320 330 340 350 360
|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
 LERRLEMTGVCASQMALTLGGPNRLNPKNVHQRPTVALLCGPHVKGAGQISCGRHLANH

370 380 390 400 410 420
|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
 DVQVILFLPNFVKMLE SITNELSLFSKTQGGVSSLKDLPTSPVDLVINCLDCPENVFLR

430 440 450 460 470 480
|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
 DQPWYKAAVAWANQNRA PVLSIDPPVHEVEQGIDAKWSLALGLPLPLGEGHAGRIYLCDIG

490 500
|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
 IPQQVFQEVGINYHSPFGCKFVIPLHSA

Supplementary figure 2: Sequence of human EDC3 with residues highlighted that potentially mimic contact site for HA binding with bNAb CR6261. The residues shaded in yellow, cyan and green are shown in similar colors in Figure 1D.