

Supplementary Information for

***Shigella* promotes major alteration of gut epithelial physiology and tissue invasion
by shutting off host intracellular transport**

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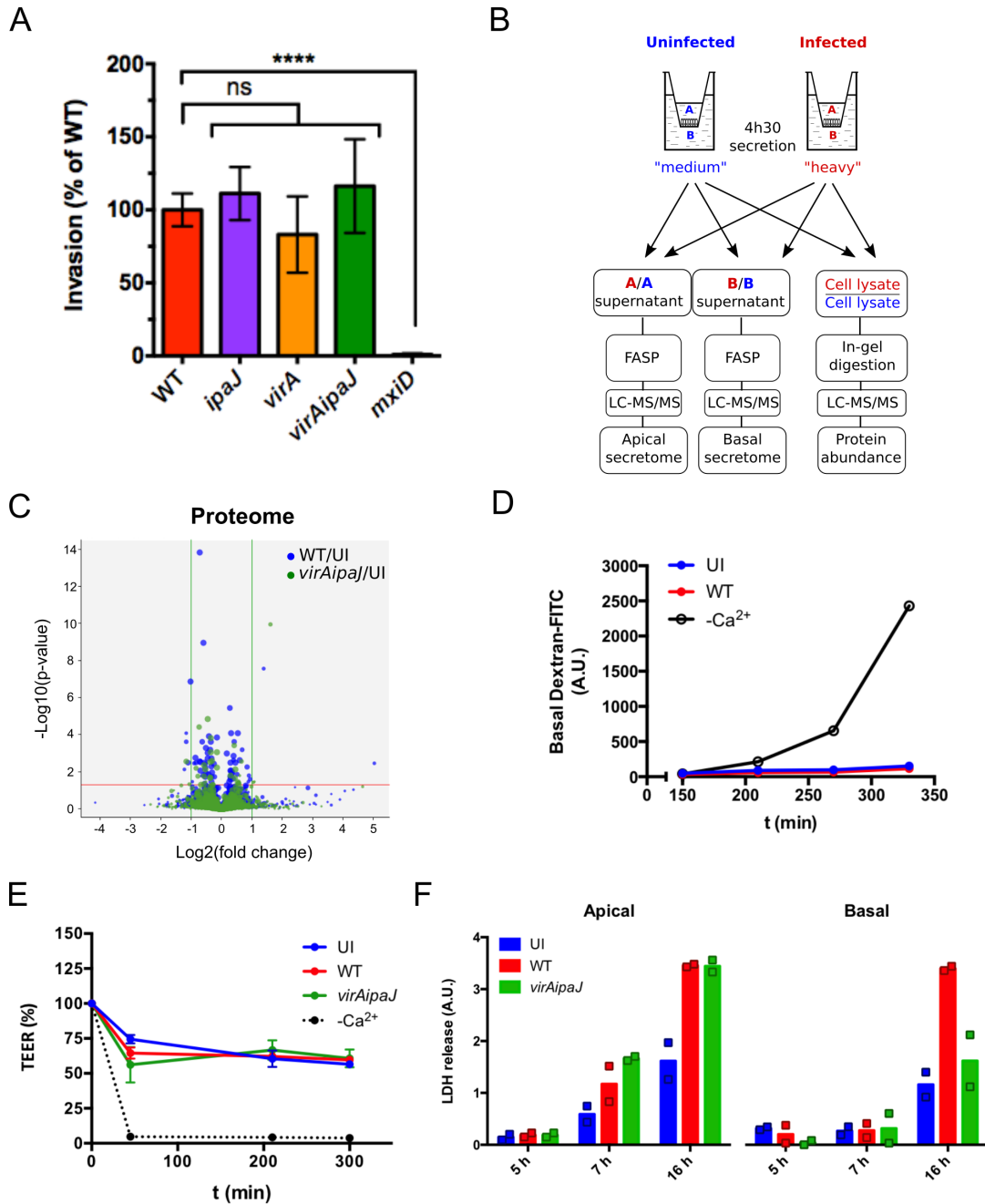


Fig. S1. (A) Gentamicin protection assay of WT in comparison with *ipaJ*, *virA*, *virAipaJ* and the non-invasive mutant *mxiD*. Mean \pm SD. n = 3. Ns: non significant; ****p<0.0001 (one-way ANOVA, Dunnett's *post-hoc* test). (B) Schematic representation of the experimental setup, proteomics workflow and data analysis of the SILAC LC-MS/MS experiment. (C) Volcano plots displaying log₂ fold change of total proteome for WT (blue) and *virAipaJ* (green) infected cells in comparison with uninfected (UI) conditions. (D-F) Dextran 70 kDa permeability (D), transepithelial electrical resistance (TEER) (E), and lactate dehydrogenase (LDH) release (F) over time in Caco-2/TC7 cells grown in transwell filters. Cells were UI, WT- or *virAipaJ*-infected, or incubated in medium without Ca²⁺ (-Ca²⁺) for (D) and (E).

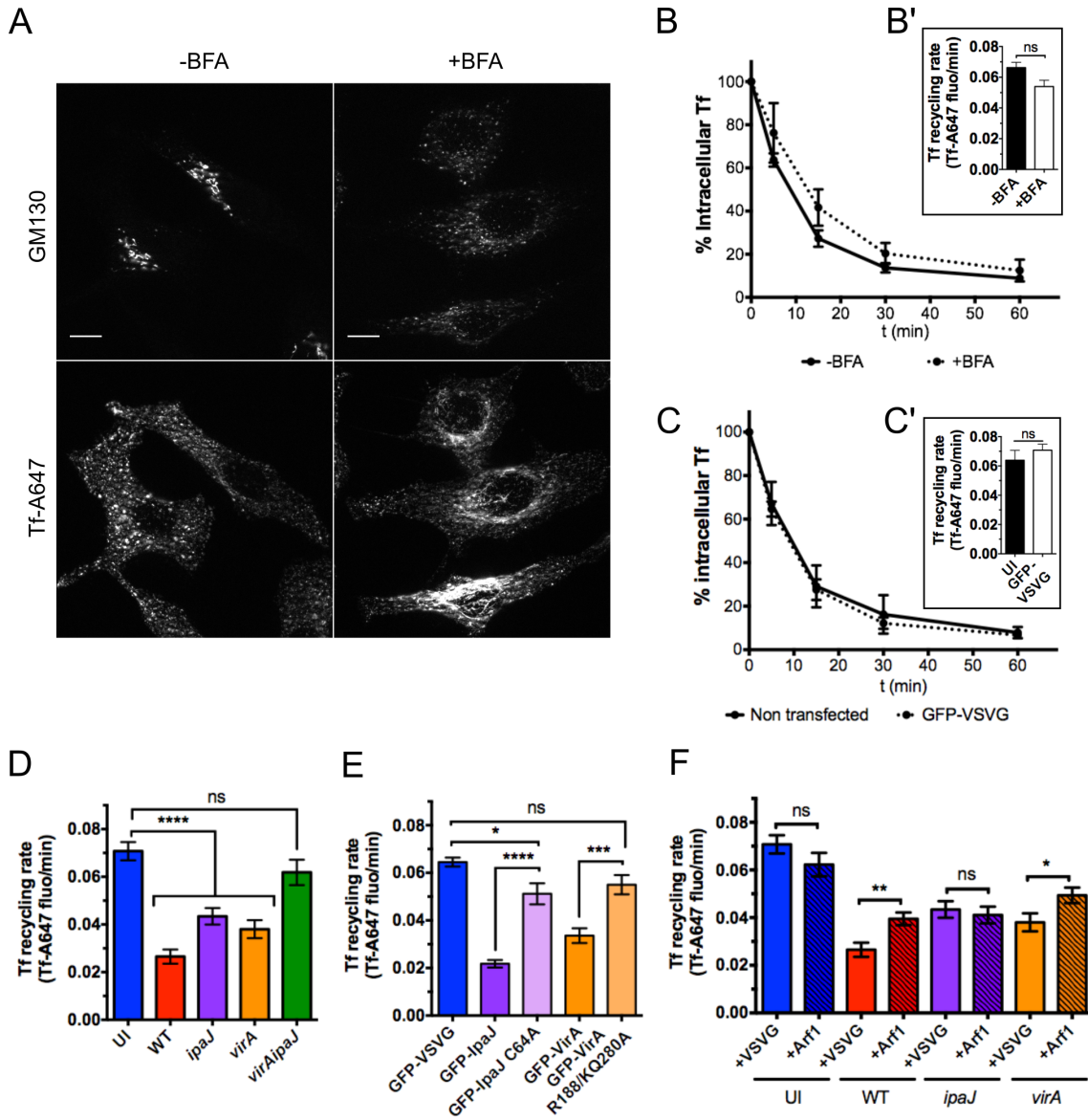


Fig. S2. (A) *Cis*-Golgi (GM130) and recycling endosomes (Tf-A647) structure upon BFA treatment. Hep2 cells were loaded with Tf-AF647 and incubated with or without BFA for 30 minutes and then stained with an anti-GM130 antibody. Scale bar: 10 μ m. (B) Tf recycling kinetics upon BFA treatment. Hep2 cells were loaded with Tf-AF647, BFA was added (+BFA) or not (-BFA) to the medium for 30 minutes and cells were then chased with the unlabeled holo-Tf for up to 60 minutes. The loss of intracellular Tf-AF647 fluorescence was monitored over-time by FC. (C) Tf-AF647 recycling kinetics in non-transfected or GFP-VSVG transfected Hep2 cells. B-C, mean \pm SD, n = 3. (B'-C') Tf recycling rates for kinetics depicted on Fig. S2B-C. Mean \pm SE. ns: non significant (unpaired two-tailed Welch's *t*-test). (D-E-F) Tf recycling rates for kinetics depicted on Fig. 2B-C-D, respectively. Mean \pm SE. ns: non significant; **p*<0.05; ***p*<0.01; ****p*<0.001; *****p*<0.0001 (D, one-way ANOVA, Dunnett's *post-hoc* test; E, one-way ANOVA, Tukey's *post-hoc* test; F, unpaired two-tailed Welch's *t*-test).

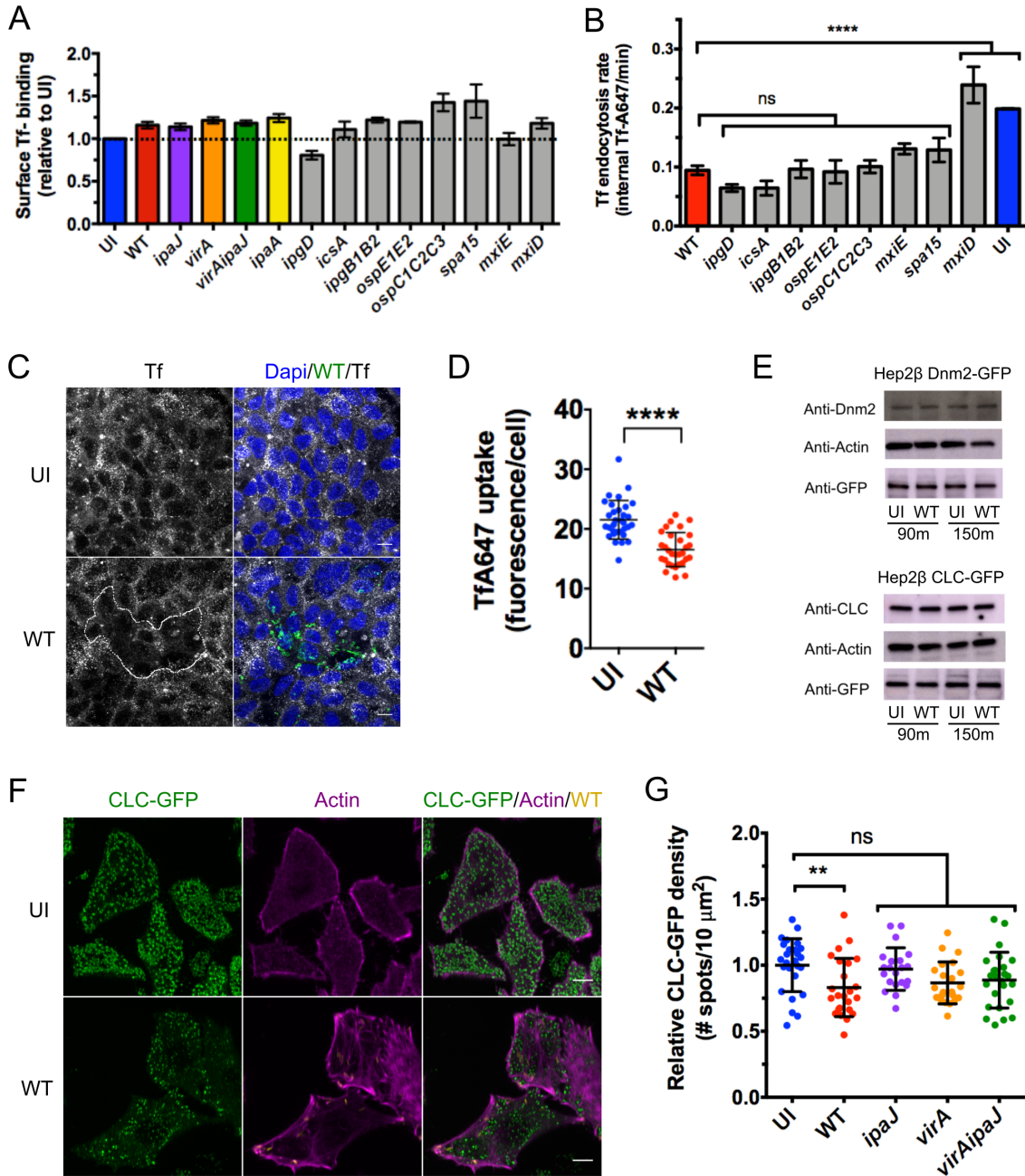


Fig. S3: (A) Surface TfR upon infection with different *S. flexneri* strains. Hep2 cells were uninfected (UI) or infected with GFP-WT or mutant strains for 90 min and then incubated at 4 °C in the presence of Tf-AF647 for 30 minutes. The total surface Tf-AF647 fluorescence was quantified by FC, and represented relative to UI conditions. Mean \pm SD, $n \geq 3$. (B) Endocytosis inhibition upon infection with different *S. flexneri* strains. Hep2 cells were left UI or infected with GFP-expressing WT or mutant strains for 90 min, prior to monitor by FC the Tf-AF647 uptake over time. The endocytosis rate was calculated during the first 5 min of kinetics. Mean \pm SD, $n \geq 3$. Ns: non significant;

**** $p < 0.0001$ (one-way ANOVA, Dunnett's *post-hoc* test). (C) Tf uptake is decreased in infected polarized cells. Caco-2/TC7 cells were grown in transwell filters up to polarization and differentiation. Cells were UI (upper panel) or challenged with WT strain (lower panel) for 4 hours. Tf-Cy3 was added to the basolateral compartment and left for 15 min at 37 °C to allow for Tf uptake, fixed and stained with Dapi and rabbit anti-LPS followed by anti-rabbit-A488. Scale bar: 10 μm . ROI: infected cells. (D) Quantification of Tf-A647 uptake on Caco-2/TC7 cells, represented as total Tf-A647 fluorescence/cell. Mean \pm SD, $n = 32$ cells in each condition, representative of two independent experiments. **** $p < 0.0001$ (Mann-Whitney test). (E) Western blots of Hep2 β Dnm2-GFP (upper panel) or Hep2 β CLC-GFP (bottom panel) of cells UI or infected for 90 or 150 minutes with WT *S. flexneri*. Cell lysates were immunoblotted with anti-Dnm2, anti-CLTA, anti-GFP and anti-Actin. (F-G) CLC-GFP density at plasma membrane. Hep2 β CLC-GFP cells were UI or infected with WT or mutant strains for 90 minutes, fixed, labeled with rabbit anti-LPS followed by anti-rabbit-A405 and Phalloidin-A647, and imaged with a confocal (F) or a TIRF (G) microscope. Scale bar: 10 μm . (G) Quantification of CLC-GFP density (number of CLC-GFP spots/area) at plasma membrane from TIRF microscopy images. Mean \pm SD. $21 < n < 27$ cells pooled from 2 independent experiments. Ns, non significant; ** $p < 0.01$ (one-way ANOVA, Dunnett's *post-hoc* test).

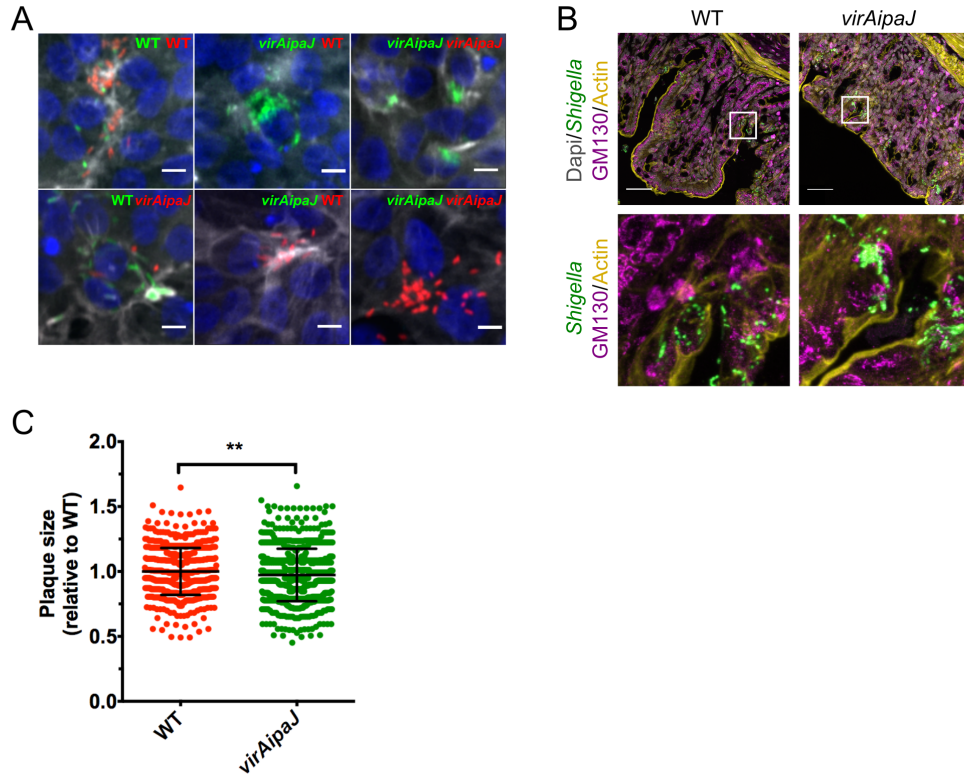


Fig. S4: (A) Caco-2/TC7 cells were primo-infected with GFP-expressing WT or *virAipaJ* strains (green) for 4 hours, and then re-infected with the same strains but expressing dsRed for 2 more hours (red). Cells were fixed and stained with Dapi (blue) and Phalloidin-AF647 (white). Scale bar: 10 μ m. (B) IpaJ and VirA induce Golgi apparatus disruption in an *in vivo* model of shigellosis. Guinea pigs were infected intrarectally with GFP-expressing WT or *virAipaJ* strains and sacrificed 4 hours post-infection. The colonic tissue was fixed, cut and labeled with anti-GM130 (*cis*-Golgi), Phalloidin-AF647 (actin) and Dapi (nuclei). Scale bars: 50 μ m. (C) Plaque assays were performed by infecting Caco-2/TC7 cell monolayers with either WT or *virAipaJ* strains for 48 hours. Mean \pm SD, n = 3 independent experiments. ** p<0.01 (unpaired two-tailed Welch's *t*-test).

Table S1: Apical and Basal secretomes of *S. flexneri* infected cells compared to uninfected cells. ID: protein identifier; WT: WT *S. flexneri* infection; UI: uninfected cells; virAipaJ: *virAipaJ* *S. flexneri* mutant; SP: signal peptide.

Apical Secretome_Less secreted							
ID	Description	log2 ratio WT/UI	p-value	log2 ratio virAipaJ/UI	p-value	SP	Protein class
Q9NR30	Nucleolar RNA helicase 2	-1.072528254	0.009176105	-0.549899695	0.543824377	-	enzyme
O00515	Ladinin-1	-0.901708044	0.020132052	-0.040926188	0.98114634	-	structural protein
O15372	Eukaryotic translation initiation factor 3 subunit H	-2.17768958	0.037502682	0.693417745	0.579838846	-	hydrolase metalloprotease
O75390	Citrate synthase, mitochondrial	-1.279822363	0.005714955	-0.933809389	0.20341321	-	lyase transferase
P15144	Aminopeptidase N	-1.696619272	0.041157819	-0.528181466	0.811421783	-	hydrolase metalloprotease
P27487	Dipeptidyl peptidase 4	-1.119890251	0.019717833	-0.116367639	0.950407398	-	enzyme modulator hydrolase
P46782	40S ribosomal protein S5	-0.876133518	0.022861358	-0.459930768	0.482225647	-	nucleic acid binding
Q14011	Cold-inducible RNA-binding protein	-0.615170382	0.04174039	-0.100689416	0.930926354	-	nucleic acid binding
Q15393	Splicing factor 3B subunit 3	-1.100422107	0.018986403	-0.354041732	0.664209046	-	nucleic acid binding
Q92484	Acid sphingomyelinase-like phosphodiesterase 3a	-2.755432112	0.029673948	-0.234737391	0.962922352	+	hydrolase
P54802	Alpha-N-acetylglucosaminidase	-2.09901404	1.08329e-13	-0.966313613	0.003282959	+	hydrolase glycosidase
P19801	Amlonide-sensitive amine oxidase [copper-containing]	-5.230349024	0.007959639	-2.174914133	0.527077691	+	oxidoreductase
P02647	Apolipoprotein A-I	-3.770306863	3.42792e-16	-1.478777761	0.002648721	+	transfer/carrier cholesterol transport stress response
P06727	Apolipoprotein A-IV	-3.916345947	2.94833e-07	-0.435649878	0.875016256	+	transfer/carrier cholesterol transport stress
P04114	Apolipoprotein B-100	-2.168899312	3.42792e-16	-0.798189399	0.005171494	+	transfer/carrier cholesterol transport
P02656	Apolipoprotein C-III	-3.952868123	0.017971834	-1.595370023	0.411587773	+	transfer/carrier lipid transport
P02649	Apolipoprotein E	-2.651775124	0.000615245	-1.222471386	0.289896353	+	cholesterol transport cell differentiation stress response
P02749	Beta-2-glycoprotein 1	-2.840928212	5.41563e-11	-1.00072888	0.005551265	+	Cell-cell adhesion signaling
P19835	Bile salt-activated lipase	-2.946806725	0.000190912	-1.512317497	0.114588885	+	hydrolase lipase
Q8NF28	Cell adhesion molecule 4	-1.663926779	0.011039695	-0.490880893	0.745206979	+	cell adhesion
P10909	Clusterin	-3.289370598	4.80282e-06	-2.361170244	0.00202787	+	enzyme
P39060	Collagen alpha-1(XVIII) chain	-1.602212468	0.037332003	0.000662118	0.999513715	+	ECM
P01034	Cystatin-C	-1.81423565	0.002690456	-0.666114156	0.358087873	+	enzyme modulator
P24855	Deoxyribonuclease-1	-3.224205165	3.24603e-05	-1.216528549	0.184676547	+	hydrolase nucleic acid binding
Q01459	Di-N-acetylchitobiase	-3.42920159	0.00567896	-1.047483268	0.553934681	+	hydrolase
P00533	Epidermal growth factor receptor	-2.674587265	1.40611e-05	-0.833914063	0.31330118	+	receptor signaling
P22455	Fibroblast growth factor receptor 4	-1.517883257	0.00127772	-1.243800291	0.01740424	+	receptor signaling
Q08380	Galectin-3-binding protein	-2.245544148	4.80282e-06	-0.032492566	0.987175607	+	cell adhesion ECM
P35052	Glypican-1	-2.60317129	2.9743e-09	-0.809684252	0.114588885	+	heparan sulfate binding
P51654	Glypican-3	-3.110516585	2.24908e-12	-1.096559712	0.000645332	+	heparan sulfate binding
Q92896	Golgi apparatus protein 1	-1.041857419	0.003268394	-0.255198414	0.735160609	+	ECM
P08581	Hepatocyte growth factor receptor	-2.90469601	0.001880556	-0.748067091	0.843235782	+	receptor signaling
Q8WWA0	Intelectin-1	-4.160799167	1.18419e-05	-1.253662182	0.448141148	+	defense/immunity
Q8WVU7	Intelectin-2	-3.354673066	7.94067e-10	-1.166277392	5.6509e-05	+	defense/immunity
P05362	Intercellular adhesion molecule 1	-1.740581759	0.000554569	0.078685369	0.964781211	+	cell adhesion ECM
O43278	Kunitz-type protease inhibitor 1	-2.213292313	5.09615e-09	-0.890337415	0.080588616	+	enzyme modulator
P01130	Low-density lipoprotein receptor	-1.828778698	0.010472209	-1.124808228	0.472513044	+	lipid transport
O75581	Low-density lipoprotein receptor-related protein 6	-2.042580795	0.03114173	-0.245697834	0.929085707	+	signaling
O00754	Lysosomal alpha-mannosidase	-1.340026936	0.000256636	-0.53437202	0.406689163	+	hydrolase glycosidase
P42785	Lysosomal Pro-X carboxypeptidase	-0.95041666	0.000999696	-0.101731223	0.919615924	+	hydrolase serine-protease
Q9H8J5	MANSC domain-containing protein 1	-2.312417389	0.000216978	-0.821504026	0.381236027	+	?
Q6UXI9	Nephronectin	-2.341609519	0.043700168	-1.257987913	0.479420882	+	cell-cell adhesion ECM
P61916	NPC intracellular cholesterol transporter 2	-2.062981637	0.000115307	-0.49529118	0.518527857	+	transfer/carrier cholesterol transport
Q98TY2	Plasma alpha-L-fucosidase	-2.899768911	3.74973e-05	-1.500273028	0.06962011	+	hydrolase glycosidase
O15031	Plexin-B2	-2.083791668	0.005040614	-0.884717667	0.479420882	+	receptor signaling
Q15113	Procollagen C-endopeptidase enhancer 1	-2.871186463	0.047670998	-1.34267566	0.561908896	+	enzyme modulator
Q07954	Prolow-density lipoprotein receptor-related protein 1	-1.572789608	8.82014e-08	-0.789571718	0.03414508	+	?
P07602	Prosaposin	-1.726286625	3.77926e-08	-0.917842143	0.001488222	+	?
P78504	Protein jagged-1	-2.655490275	0.000115176	-0.792980521	0.24438053	+	signaling
O00584	Ribonuclease T2	-3.007530685	0.047294455	-1.430674438	0.490124737	+	enzyme
Q9UGT4	Sushi domain-containing protein 2	-0.828972816	0.01739049	0.095736124	0.945593165	+	defense/immunity
P04066	Tissue alpha-L-fucosidase	-2.449846813	5.35154e-05	-0.8962332	0.334821933	+	hydrolase glycosidase
O00300	Tumor necrosis factor receptor superfamily member 11B	-5.062178219	0.001963304	-0.916293698	0.648849883	+	receptor defense/immunity
Q03405	Urokinase plasminogen activator surface receptor	-3.813992228	6.13582e-07	-1.25186322	0.047391062	+	receptor
P07225	Vitamin K-dependent protein S	-4.474216837	2.54396e-10	-1.420369843	0.016132286	+	enzyme modulator
P04004	Vitronectin	-2.982579992	0.000197241	-1.11602366	0.310312981	+	cell adhesion

O00462	Beta-mannosidase	-2.702760859	0.002410331	-1.127260251	0.226669752	+	hydrolase glycosidase
O00468	Agtrin	-1.737747334	3.70417e-05	-0.475806507	0.55248196	+	ECM enzyme modulator receptor
O14773	Tripeptidyl-peptidase 1	-2.631882179	0.000915453	-1.00872291	0.518527857	+	hydrolase serine-protease
O43895	Xaa-Pro aminopeptidase 2	-1.53625792	0.001608684	-0.56608487	0.612391974	+	hydrolase nucleic acid binding metalloprotease
O75326	Semaphorin-7A	-3.539691041	2.38471e-16	-1.344262748	0.000163093	+	signaling
O75882	Attractin	-3.506429141	1.76588e-15	-0.807751537	0.181248181	+	ECM enzyme modulator receptor
O75976	Carboxypeptidase D	-1.509654772	0.001699526	-1.1294363	0.034065376	+	hydrolase
O94985	Calsyntenin-1	-3.161074006	0.000990967	-1.001102039	0.338201356	+	Ca binding cell adhesion
P00450	Ceruloplasmin	-4.26040362	0.001749595	-1.333213422	0.334821933	+	oxidoreductase
P00734	Prothrombin	-5.521919139	4.57527e-06	-1.837239314	0.068742229	+	hydrolase
P00742	Coagulation factor X	-4.508410734	0.000148666	-0.60204236	0.8172103	+	hydrolase
P00751	Complement factor B	-2.862149116	2.00228e-06	-0.854005705	0.349027168	+	hydrolase serin-protease
P01009	Alpha-1-antitrypsin	-3.814094495	1.69706e-22	-1.22669808	0.002879415	+	hydrolase
P01019	Angiotensinogen	-4.089063862	2.80835e-14	-0.836024591	0.339487412	+	hydrolase
P01033	Metalloproteinase inhibitor 1	-3.537151001	0.000220074	-1.556984196	0.200956399	+	enzyme modulator
P01042	Kinogen-1	-3.336751227	5.58542e-07	-0.957204588	0.379581202	+	enzyme modulator
P02675	Fibrinogen beta chain	-2.900053829	1.81789e-05	-1.105811058	0.187612576	+	signaling
P02679	Fibrinogen gamma chain	-2.650129695	0.005099706	-0.248842688	0.945593165	+	signaling
P02751	Fibronectin	-2.892777969	8.12678e-08	-0.795085642	0.31330118	+	signaling
P02753	Retinol-binding protein 4	-2.465348497	1.6744e-05	-1.000450291	0.238713661	+	transfer/carrier
P02765	Alpha-2-HS-glycoprotein	-3.435548473	4.63006e-08	-0.642925268	0.569813023	+	enzyme modulator
P02766	Transhyretin	-4.169509128	2.98341e-07	-0.184429086	0.959155064	+	transfer/carrier transporter
P02768	Serum albumin	-3.518172947	1.94206e-18	-0.943331156	0.024246672	+	transfer/carrier
P02771	Alpha-fetoprotein	-3.626089192	1.14551e-20	-1.41259489	0.003931815	+	transfer/carrier
P02790	Hemopexin	-4.816256767	0.026155772	-2.061239254	0.518527857	+	hydrolase
P05067	Amyloid beta A4 protein	-4.098788616	0.002075131	-1.091378053	0.518527857	+	enzyme modulator
P06865	Beta-hexosaminidase subunit alpha	-2.367092607	1.10004e-05	-0.120954044	0.959155064	+	hydrolase glycosidase
P07339	Cathepsin D	-1.370392365	0.001796267	0.48495812	0.664209046	+	hydrolase
P07686	Beta-hexosaminidase subunit beta	-1.683284597	0.000119003	-0.805910193	0.195562828	+	hydrolase glycosidase
P07858	Cathepsin B	-1.775831189	0.037502682	-0.838183895	0.472513044	+	hydrolase enzyme modulator
P08582	Melanotransferrin	-2.370202386	1.6525e-14	-1.177250479	0.000859465	+	receptor hydrolase transfer/carrier
P08709	Coagulation factor VII	-3.312701112	0.000470211	-1.004325085	0.187612576	+	hydrolase
P09923	Intestinal-type alkaline phosphatase	-1.276369818	0.001688077	-0.736140993	0.226669752	+	hydrolase phosphatase
P10253	Lysosomal alpha-glycosidase	-2.16482629	5.90379e-08	-0.588326261	0.289896353	+	hydrolase glucosidase
P10586	Receptor-type tyrosine-protein phosphatase F	-2.520160293	7.31133e-05	-1.249503795	0.151557305	+	hydrolase phosphatase receptor
P10619	Lysosomal protective protein	-2.35202299	1.25516e-05	-0.809098881	0.176132719	+	hydrolase serine-protease
P11047	Laminin subunit gamma-1	-1.484704514	0.000375096	-0.665986972	0.289896353	+	ECM enzyme modulator receptor
P12109	Collagen alpha-1(V) chain	-3.384465418	1.82797e-19	-1.575274609	1.75946e-05	+	receptor
P12821	Angiotensin-converting enzyme	-1.228117154	0.003353497	-1.174052546	0.015887469	+	hydrolase metalloprotease
P14384	Carboxypeptidase M	-3.565776795	0.003796372	-0.574012752	0.695821732	+	hydrolase metalloprotease
P15289	Arylsulfatase A	-0.951970901	0.000290899	-0.414648239	0.289896353	+	hydrolase
P15586	N-acetylglucosamine-6-sulfatase	-2.678659866	5.8224e-05	-0.49240207	0.761288285	+	hydrolase
P16035	Metalloproteinase inhibitor 2	-2.445567144	0.000588368	-2.207155685	0.007622135	+	enzyme modulator
P22692	Insulin-like growth factor-binding protein 4	-4.981841233	0.036464109	-1.16650411	0.843235782	+	enzyme modulator
P40189	Interleukin-6 receptor subunit beta	-3.676661887	0.000784446	-2.490746978	0.01825217	+	defense/immunity
P48052	Carboxypeptidase A2	-4.074445483	5.24827e-06	-1.651946586	0.016132286	+	hydrolase
P53634	Dipeptidyl peptidase 1	-3.163421105	7.34655e-07	-0.708798112	0.518527857	+	hydrolase enzyme modulator
P98160	Basement membrane-specific heparan sulfate proteoglycan core protein	-2.456713199	2.51835e-08	-1.855418827	5.6509e-05	+	ECM enzyme modulator receptor
Q02818	Nucleobindin-1	-1.800173348	4.5499e-05	-0.661131282	0.231377562	+	Ca binding nucleic acid binding
Q06481	Amyloid-like protein 2	-2.496441105	3.58965e-05	-1.050859474	0.289896353	+	enzyme modulator
Q08431	Lactadherin	-3.626715751	7.78487e-06	-1.287136198	0.114588885	+	cell adhesion hydrolase receptor
Q13421	Mesothelin	-2.557540302	0.006728528	-1.130892643	0.212438552	+	ECM
Q13443	Disintegrin and metalloproteinase domain-containing protein 9	-3.266587756	0.006212622	-0.831811042	0.605128176	+	hydrolase metalloprotease
Q15582	Transforming growth factor-beta-induced protein ig-h3	-2.512671218	0.033128595	-1.239638028	0.37344535	+	cell adhesion signaling
Q15904	V-type proton ATPase subunit S1	-2.478891712	0.000779695	-1.36078358	0.206790838	+	hydrolase transporter
Q16819	Meprin A subunit alpha	-3.567380956	1.69706e-22	-0.989699422	0.002648721	+	hydrolase
Q86504	G-protein coupled receptor 126	-2.530405276	0.005795046	-1.544077127	0.145339862	+	defense/immunity receptor
Q8NHP8	Putative phospholipase B-like 2	-1.338750265	0.039704778	-0.869689603	0.289896353	+	hydrolase
Q92673	Sortilin-related receptor	-2.029496346	3.59781e-08	-0.182637689	0.929085707	+	receptor transporter
Q92820	Gamma-glutamyl hydrolase	-3.221545027	0.005354742	-0.858703609	0.750257531	+	hydrolase
Q92876	Kallikrein-6	-2.515135245	0.044326751	-1.240457088	0.431931219	+	hydrolase

Q99519	Sialidase-1	-2.630696969	0.012832485	-2.029647075	0.22939228	+	hydrolase
Q99523	Sortilin	-1.59966745	0.000256636	-0.353783914	0.579838846	+	receptor transporter
Q9BQ57	Hephaestin	-1.421112217	4.15775e-05	-0.45456352	0.518527857	+	oxidoreductase
Q9BYF1	Angiotensin-converting enzyme 2	-3.302852067	4.03175e-22	-1.018030793	0.002055761	+	hydrolase metalloprotease
Q9H3G5	Probable serine carboxypeptidase CPVL	-2.596663421	0.001880556	-0.880312381	0.579838846	+	hydrolase serine-protease
Q9HAT2	Sialate O-acetyltransferase	-1.772307888	0.044326751	-1.596588246	0.289896353	+	hydrolase
Q9UHL4	Dipeptidyl peptidase 2	-1.656231073	0.005714955	-0.68055341	0.491090231	+	hydrolase
Q9UNN8	Endothelial protein C receptor	-2.817000663	0.012507399	-0.43351713	0.875737994	+	enzyme modulator receptor

Basal Secretome_Less secreted

ID	Description	log2 ratio WT/Ut	p-value	log2 ratio virAipa/Ut	p-value	SP	Protein class
P08758	Annexin A5	-1.62801464	0.018622276	-1.158172856	0.185670339	-	enzyme regulator signal transduction
Q8NB34	Golgi membrane protein 1	-1.092986292	0.010143159	-0.572540669	0.231509058	-	?
P08727	Keratin, type I cytoskeletal 19	-2.074858939	0.00059044	0.013379057	0.98687303	-	structural
Q8WVQ1	Soluble calcium-activated nucleotidase 1	-1.797250458	0.000620701	-0.576670255	0.203638165	-	hydrolase
O60513	Beta-1,4-galactosyltransferase 4	-1.486800427	0.011859212	-0.350438985	0.607937785	-	transferase
P05023	Sodium/potassium-transporting ATPase subunit alpha-1	-0.990374016	0.002142764	-2.048518046	7.54839e-07	-	transporter hydrolase
P06576	ATP synthase subunit beta, mitochondrial	-0.87880808	0.049391134	-1.11937592	0.075205165	-	hydrolase Nucleic acid binding transporter
P06753	Tropomyosin alpha-3 chain	-0.813900575	0.003205936	-0.422885876	0.127155705	-	cytoskeletal
P09493	Tropomyosin alpha-1 chain	-0.796639221	0.026836656	-0.379725908	0.360428637	-	cytoskeletal
P09622	Dihydropyridyl dehydrogenase, mitochondrial	-0.825620308	0.013899356	-0.421066649	0.277249395	-	oxidoreductase
P13798	Acylamino-acid-releasing enzyme	-0.972970757	0.000596326	-0.127096769	0.767547783	-	hydrolase
P19105	Myosin regulatory light chain 12A	-1.572688615	0.014266744	-0.877480378	0.202054219	-	cytoskeletal ca binding
Q15043	Zinc transporter ZIP14	-0.97384405	0.000777029	-0.200727336	0.497172595	-	transporter
Q99674	Cell growth regulator with EF hand domain protein 1	-2.338144571	0.000289998	-0.658818557	0.165386152	-	transporter
Q9H8J5	MAN5C domain-containing protein 1	-0.685391203	0.02304981	-0.469465831	0.1609184	+	?
P54802	Alpha-N-acetylglucosaminidase	-1.210866266	0.001363294	-1.569381066	0.00028594	+	hydrolase glycosidase
P19801	Amiloride-sensitive amine oxidase [copper-containing]	-1.271825603	0.00046389	-1.243707141	0.002538863	+	oxidoreductase
P06727	Apolipoprotein A-IV	-1.562850238	0.014956961	-1.171540764	0.097779631	+	transporter/carrier cholesterol transport stress response
P19835	Bile salt-activated lipase	-1.540842913	0.003754753	-0.837336132	0.127155705	+	hydrolase lipase cell adhesion
Q99795	Cell surface A33 antigen	-1.121572889	0.0172936	-0.867944876	0.100466639	+	signaling (putative)
P00751	Complement factor B	-1.749108182	0.000596326	-1.015130791	0.070322958	+	hydrolase serin protease immunity
P78310	Coxsackievirus and adenovirus receptor	-1.800415874	0.034355278	-0.902911247	0.220028769	+	receptor cell adhesion
P01034	Cystatin-C	-2.90377613	0.000161382	0.397172402	0.691030219	+	enzyme regulator
Q9NZV1	Cysteine-rich motor neuron 1 protein	-2.122951301	0.002864811	-0.819709241	0.228598539	+	signaling
Q01459	Di-N-acetylchitobiase	-1.893577477	0.000796033	-1.118667886	0.021516508	+	hydrolase glycosidase
Q9UBP4	Dickkopf-related protein 3	-2.464894632	0.004910362	-1.2170037	0.158665628	+	signaling
Q8N8Z6	Discoidin, CUB and LCCL domain-containing protein 1	-1.6425231	0.014498196	-0.681111973	0.42302454	+	?
Q9Y2E5	Epididymis-specific alpha-mannosidase	-1.116309872	0.000133369	-0.737419392	0.00949202	+	hydrolase glycosidase
P02671	Fibrinogen alpha chain	-0.949492913	0.048730548	-1.034629453	0.026309113	+	immunity hemostasis
P23142	Fibulin-1	-2.626513039	0.003480327	-1.329534406	0.064177939	+	ECM
Q08380	Galectin-3-binding protein	-1.462942258	0.000320941	-0.650814036	0.146435561	+	cell adhesion ECM
Q16270	Insulin-like growth factor-binding protein 7	-1.702605284	0.032101957	-0.794264778	0.39306042	+	cell adhesion signaling
Q8WWA0	Intelectin-1	-1.683808916	0.02430003	-1.185428743	0.154823206	+	immunity
Q9Y624	Junctional adhesion molecule A	-1.495981913	0.037008294	0.306638252	0.74006391	+	cell adhesion
P02750	Leucine-rich alpha-2-glycoprotein	-1.132476439	0.02297713	-0.959668734	0.078331147	+	signaling?
O75581	Low-density lipoprotein receptor-related protein 6	-0.806011079	0.026174915	0.124338725	0.782556882	+	signaling
Q9BRK3	Matrix-remodeling-associated protein 8	-1.463346939	0.046295635	0.418714295	0.686256242	+	?
Q9UNW1	Multiple inositol polyphosphate phosphatase 1	-1.098464469	0.003433909	-0.421408531	0.309399832	+	hydrolase
O14786	Neuropilin-1	-1.388523405	0.008139612	-1.260753549	0.013392613	+	signaling receptor
Q15113	Procollagen C-endopeptidase enhancer 1	-2.089968084	0.000446516	-1.178828189	0.09217552	+	enzyme regulator
P28300	Protein-lysine 6-oxidase	-2.162479663	0.000132743	-0.588570107	0.257285049	+	oxidoreductase
O75787	Renin receptor	-2.741396474	0.021822359	-1.340245491	0.288971213	+	receptor
P07996	Thrombospondin-1	-1.318553234	0.001061939	-0.913750815	0.035617791	+	cell adhesion
P07225	Vitamin K-dependent protein 5	-2.07529797	0.000345722	-0.759202205	0.254577406	+	enzyme regulator
P25311	Zinc-alpha-2-glycoprotein	-2.263707686	0.000495561	-1.325405443	0.025306466	+	transporter
O60844	Zymogen granule membrane protein 16	-1.001200637	0.049747749	-1.280860913	0.027117594	+	transporter

O14773	Tripeptidyl-peptidase 1	-0.987006362	0.031180347	0.254912755	0.655641709	+	hydrolase
O15230	Laminin subunit alpha-5	-1.061541332	0.016169403	-1.148727406	0.025306466	+	ECM enzyme regulator receptor
O75882	Attractin	-1.63959283	0.00059044	-0.107970969	0.877939664	+	ECM enzyme regulator receptor
O75976	Carboxypeptidase D	-0.647466752	0.005770614	-0.456306554	0.114190332	+	hydrolase
O95633	Follistatin-related protein 3	-2.538103547	0.002614623	-0.382379001	0.656276059	+	enzyme modulator
P00742	Coagulation factor X	-1.929494089	0.045488116	-0.577528019	0.552225236	+	hydrolase
P01019	Angiotensinogen	-1.290813122	0.000163361	-0.516221069	0.200146814	+	enzyme modulator
P01033	Metalloproteinase inhibitor 1	-1.781791112	0.018627212	-0.62222561	0.480386978	+	enzyme modulator
P02766	Transthyretin	-2.076699212	0.033490097	-2.322213792	0.019549423	+	transfer/carrier transporter
P02771	Alpha-fetoprotein	-1.445966818	0.000737818	-1.482357766	0.002015158	+	transfer/carrier
P05067	Amyloid beta A4 protein	-2.079392488	0.003067314	-0.601325911	0.565656753	+	enzyme modulator
P06865	Beta-hexosaminidase subunit alpha	-0.812617059	0.014494741	-0.73827602	0.047649743	+	hydrolase
P07942	Laminin subunit beta-1	-0.714375975	0.040280202	-0.74279563	0.078331147	+	ECM enzyme regulator receptor
P10253	Lysosomal alpha-glucosidase	-0.894254227	0.006109331	-0.617752675	0.143375231	+	hydrolase
P10619	Lysosomal protective protein	-0.925473476	0.003590439	-0.553188976	0.03436407	+	hydrolase
P13497	Bone morphogenetic protein 1	-1.872013616	0.000769331	-1.502142298	0.009733934	+	hydrolase
P19957	Elafin	-1.092446328	0.000101089	-0.136414544	0.527664445	+	enzyme modulator
P26927	Hepatocyte growth factor-like protein	-1.675360956	0.002350559	-0.332811967	0.607937785	+	hydrolase
P29122	Proprotein convertase subtilisin/kexin type 6	-1.607945402	0.001169361	-0.025941328	0.963847805	+	hydrolase
P29622	Kallistatin	-1.564734637	0.028003975	-0.603306225	0.391648171	+	enzyme modulator
P42785	Lysosomal Pro-X carboxypeptidase	-0.979644156	0.000184454	-0.384506238	0.118436167	+	hydrolase
Q06481	Amyloid-like protein 2	-3.650465749	0.000238744	-0.233373086	0.862810356	+	enzyme modulator
Q06828	Fibromodulin	-2.378853667	0.003005031	-1.528915042	0.054697255	+	hydrolase
Q12913	Receptor-type tyrosine-protein phosphatase eta	-2.521355719	0.01182516	-1.008950738	0.314298615	+	hydrolase
Q13214	Semaphorin-3B	-1.660290797	0.000954431	-1.650853799	0.002574994	+	signaling
Q15582	Transforming growth factor-beta-induced protein ig-h3	-1.879888923	0.030695926	-1.141606834	0.181513283	+	cell adhesion signaling
Q6PCB0	von Willebrand factor A domain-containing protein 1	-1.493920127	0.000173389	-1.379034416	0.000870371	+	receptor
Q865Q4	G-protein coupled receptor 126	-2.041882281	0.004831223	-0.573639426	0.424571009	+	defense/immunity hydrolase receptor
Q92820	Gamma-glutamyl hydrolase	-0.968491723	0.021502437	-0.900015849	0.056356608	+	hydrolase
Q92824	Proprotein convertase subtilisin/kexin type 5	-1.905747126	0.002562959	-1.963914565	0.001803598	+	hydrolase
Q9G2M7	Tubulointerstitial nephritis antigen-like	-1.714995157	0.015403442	-0.882040597	0.23541511	+	hydrolase enzyme modulator
Q9UJ9	N-acetylglucosamine-1-phosphotransferase subunit gamma	-1.474068362	0.005256764	-1.757722546	0.001494984	+	enzyme modulator transferase