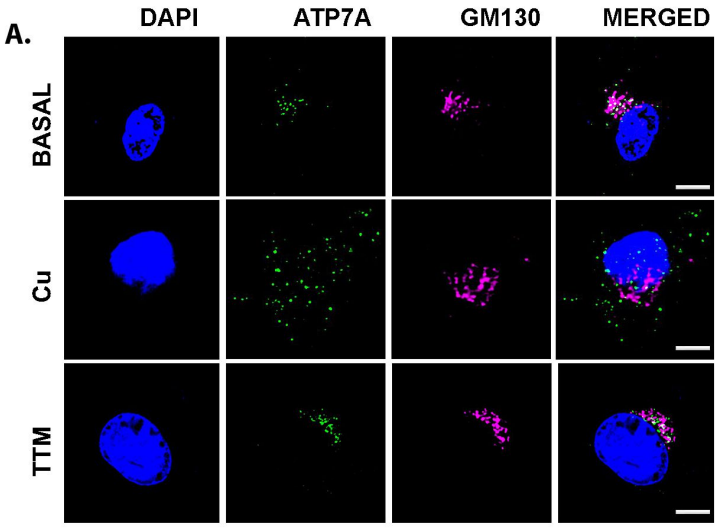
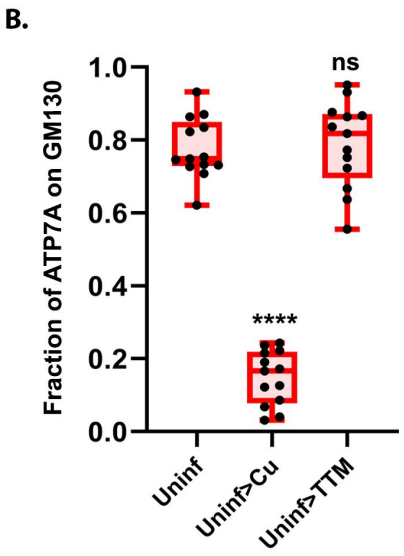
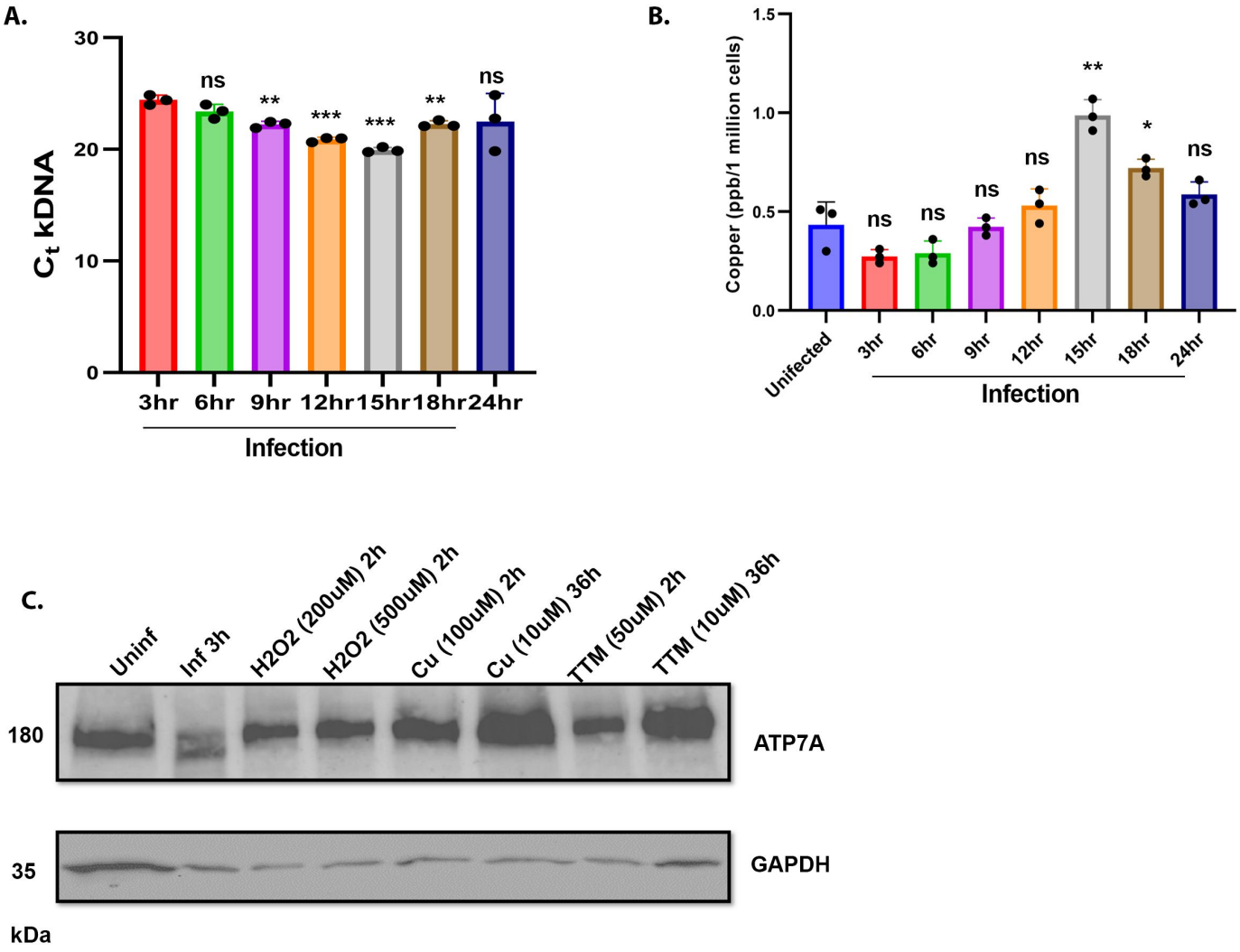
S1.

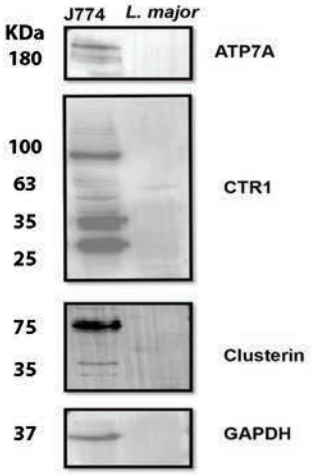

A.
DAPI
ATP7A
GM130
MERGED
BASAL
Cu
TTM


B.
Fraction of ATP7A on GM130
1.0
0.8
0.6
0.4
0.2
0.0
ns
****
Uninf
Uninf>Cu
Uninf>TTM

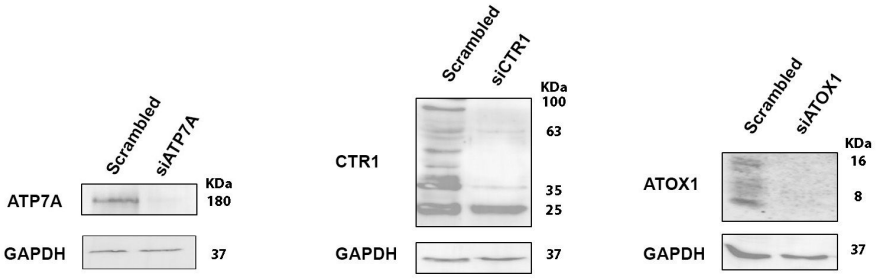
S2.


A.
30
20
10
0
C_t kDNA
ns
**
***
***
**
ns
3hr 6hr 9hr 12hr 15hr 18hr 24hr
Infection
B.
1.5
1.0
0.5
0.0
Copper (ppb/1 million cells)
ns
ns
ns
ns
**
*
ns
Unifected
3hr
6hr
9hr
12hr
15hr
18hr
24hr
Infection
C.
Uninf
Inf 3h
H2O2 (200uM) 2h
H2O2 (500uM) 2h
Cu (100uM) 2h
Cu (10uM) 36h
TTM (50uM) 2h
TTM (10uM) 36h
180
ATP7A
35
GAPDH
kDa

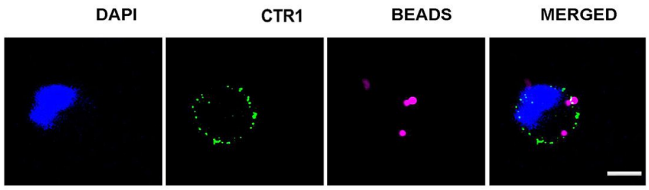
S3.


J774
L. major
KDa
180
ATP7A
100
63
35
25
CTR1
75
35
Clusterin
37
GAPDH

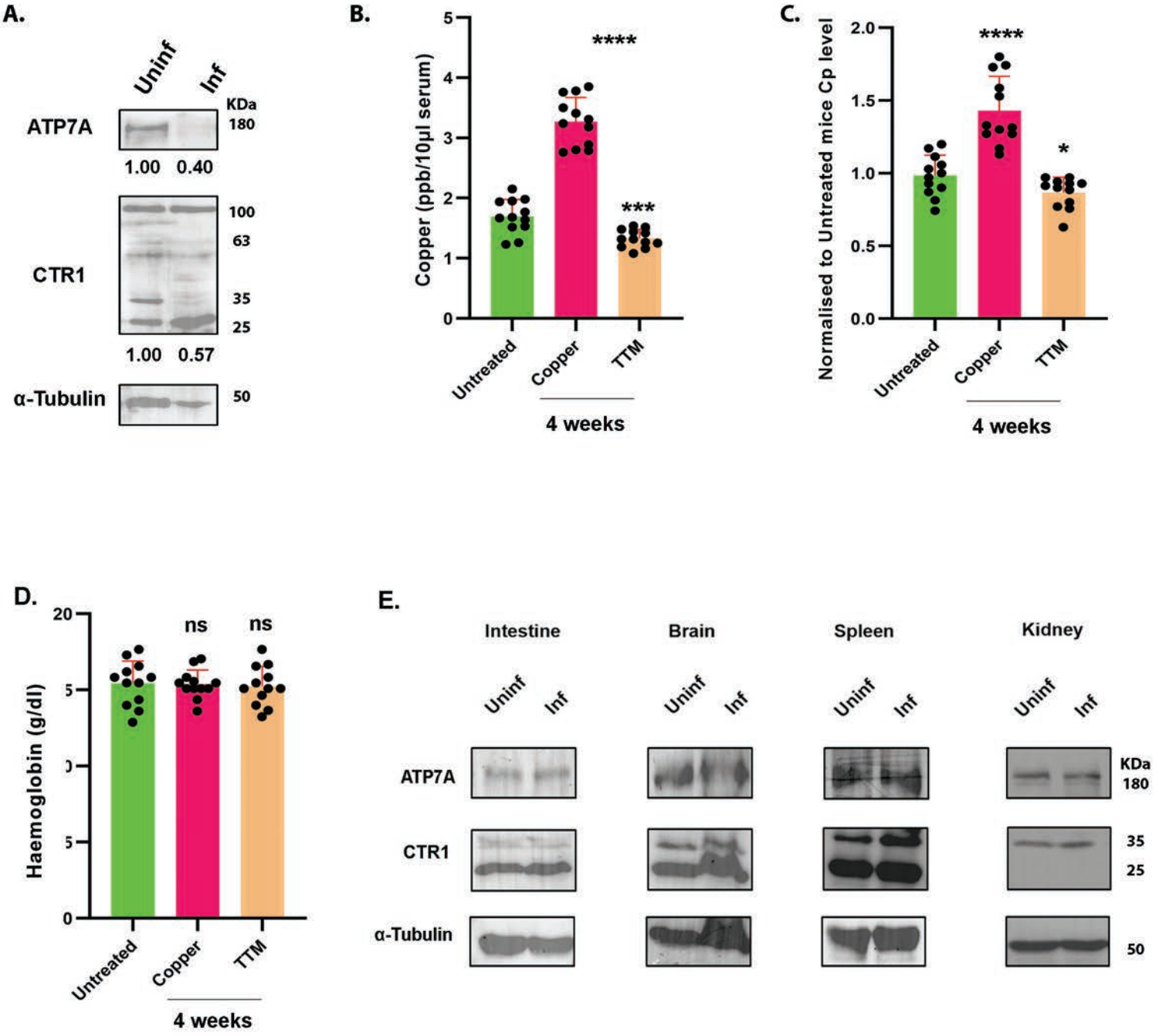
S4.


Scrambled
siATP7A
ATP7A
KDa
180
GAPDH
37
Scrambled
siCTR1
CTR1
KDa
100
63
35
25
GAPDH
37
Scrambled
siATOX1
ATOX1
KDa
16
8
GAPDH
37

S5.



S6.


A.
Uninf
Inf
KDa
ATP7A
180
1.00 0.40
100
63
CTR1
35
25
1.00 0.57
α-Tubulin
50
B.
Copper (ppb/10µl serum)
****
***
Untreated
Copper
TTM
4 weeks
C.
Normalised to Untreated mice Cp level
****
*
Untreated
Copper
TTM
4 weeks
D.
Haemoglobin (g/dl)
ns
ns
Untreated
Copper
TTM
4 weeks
E.
Intestine
Brain
Spleen
Kidney
Uninf
Inf
ATP7A
CTR1
α-Tubulin
KDa
180
35
25
50

S7.

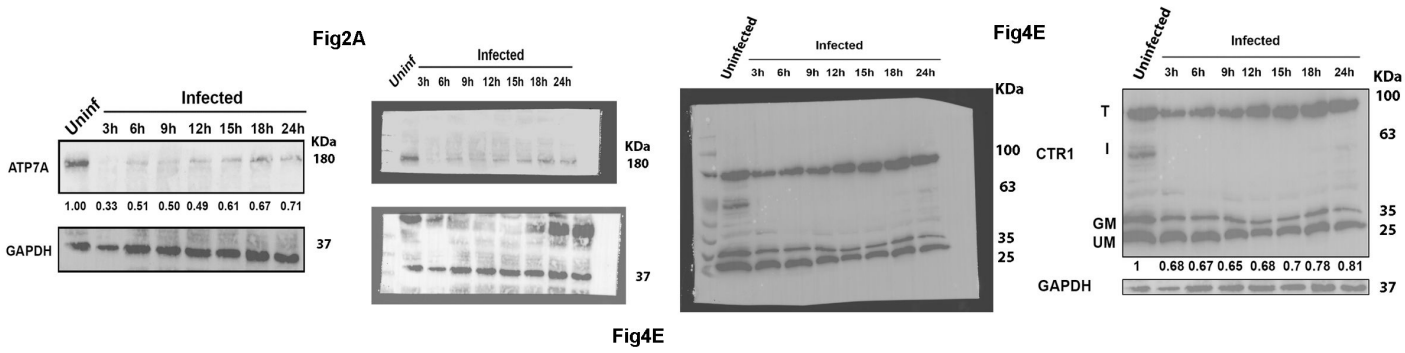


Fig2A
Uninf
Infected
3h 6h 9h 12h 15h 18h 24h
KDa
ATP7A
180
1.00 0.33 0.51 0.50 0.49 0.61 0.67 0.71
GAPDH
37
Uninf
Infected
3h 6h 9h 12h 15h 18h 24h
KDa
180
37
Uninfected
Infected
3h 6h 9h 12h 15h 18h 24h
KDa
100
63
35
25
Fig4E
Uninfected
Infected
3h 6h 9h 12h 15h 18h 24h
KDa
100
63
35
25
CTR1
T
I
GM
UM
1 0.68 0.67 0.65 0.68 0.7 0.78 0.81
GAPDH
37

Fig4E

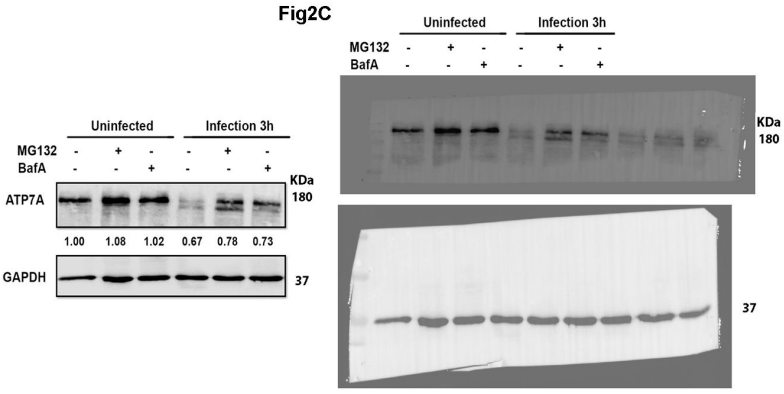


Fig2C
Uninfected
Infection 3h
MG132 - + - - + -
BafA - - + - - +
KDa
180
ATP7A
1.00 1.08 1.02 0.67 0.78 0.73
GAPDH
37
Uninfected
Infection 3h
MG132 - + - - + -
BafA - - + - - +
KDa
180
37

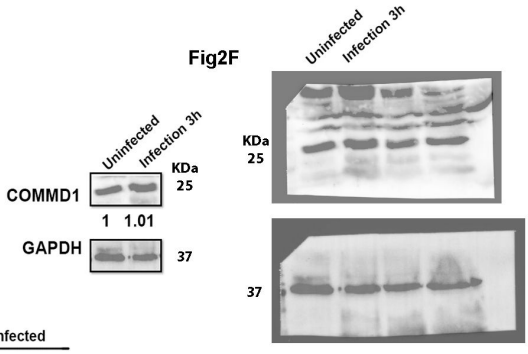


Fig2F
Uninfected
Infection 3h
KDa
25
COMMD1
1 1.01
GAPDH
37
Uninfected
Infection 3h
KDa
25
37

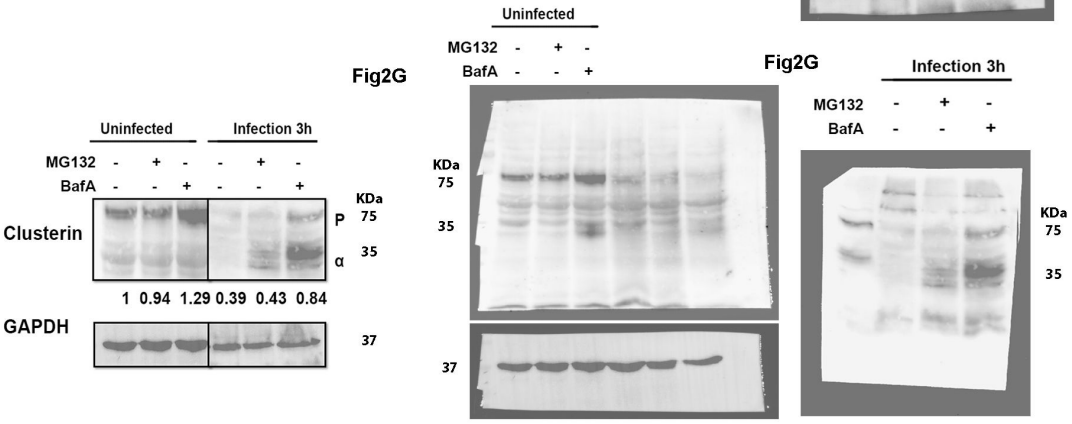
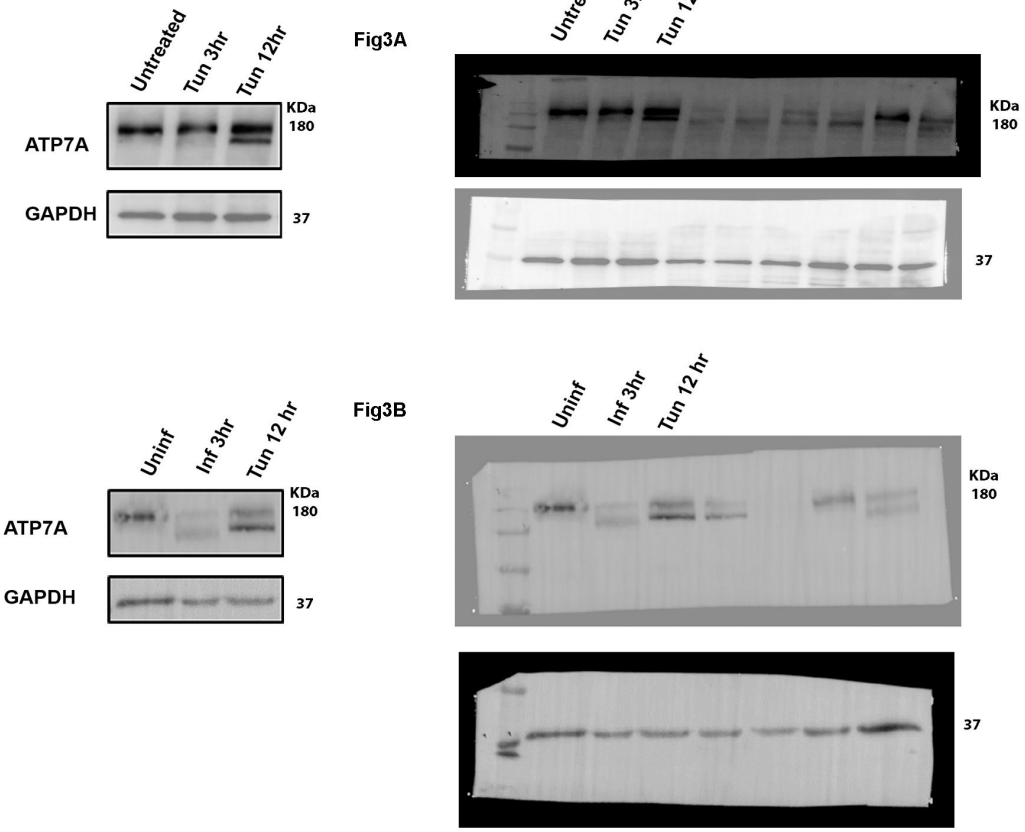


Fig2G
Uninfected
Infection 3h
MG132 - + - - + -
BafA - - + - - +
KDa
Clusterin
P
α
75
35
1 0.94 1.29 0.39 0.43 0.84
GAPDH
37
Uninfected
MG132 - + -
BafA - - +
KDa
75
35
37
Fig2G
Infection 3h
MG132 - + -
BafA - - +
KDa
75
35


Untreated
Tun 3hr
Tun 12hr
ATP7A
GAPDH
KDa
180
37
Fig3A
Uninf
Inf 3hr
Tun 12 hr
Fig3B
Untreated
PNGase 1hr
Fig3C
Uninfected
Infection 3hr
ATOX1
16
8
1
0.97
Fig4D

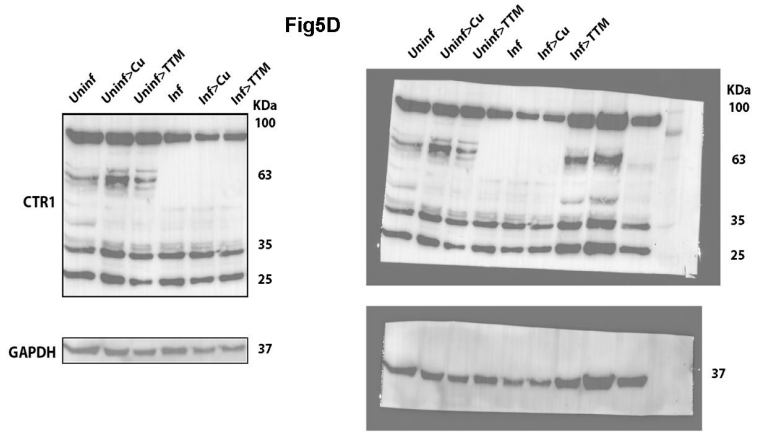


Fig5D
Uninf
Uninf>Cu
Uninf>TTM
Inf
Inf>Cu
Inf>TTM
KDa
100
63
35
25
CTR1
GAPDH
37

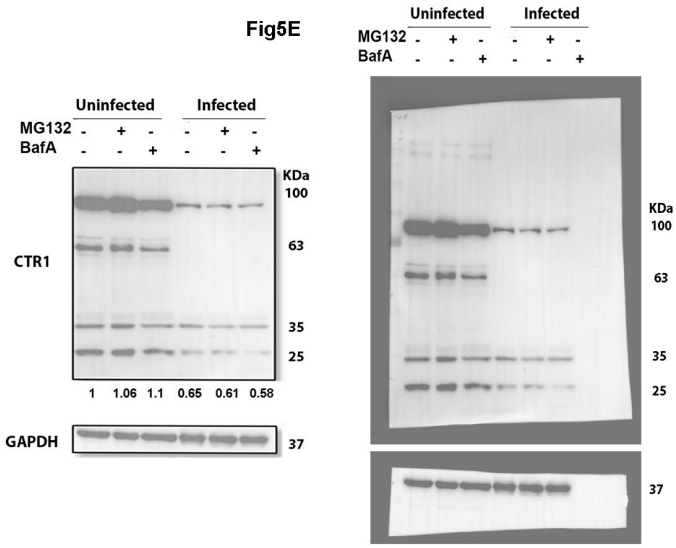


Fig5E
Uninfected
Infected
MG132
BafA
KDa
100
63
35
25
CTR1
1
1.06
1.1
0.65
0.61
0.58
GAPDH
37

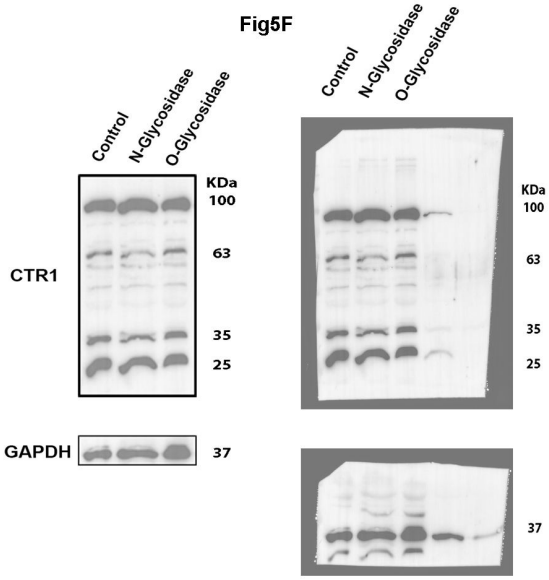


Fig5F
Control
N-Glycosidase
O-Glycosidase
KDa
100
63
35
25
CTR1
GAPDH
37

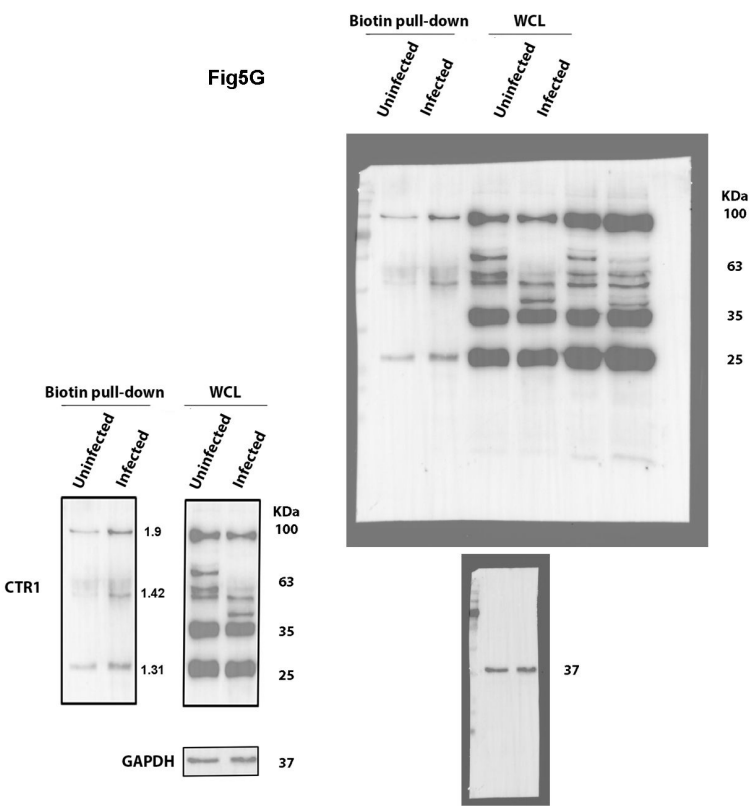


Fig5G
Biotin pull-down
WCL
Uninfected
Infected
KDa
100
63
35
25
1.9
1.42
1.31
CTR1
GAPDH
37

Fig6J

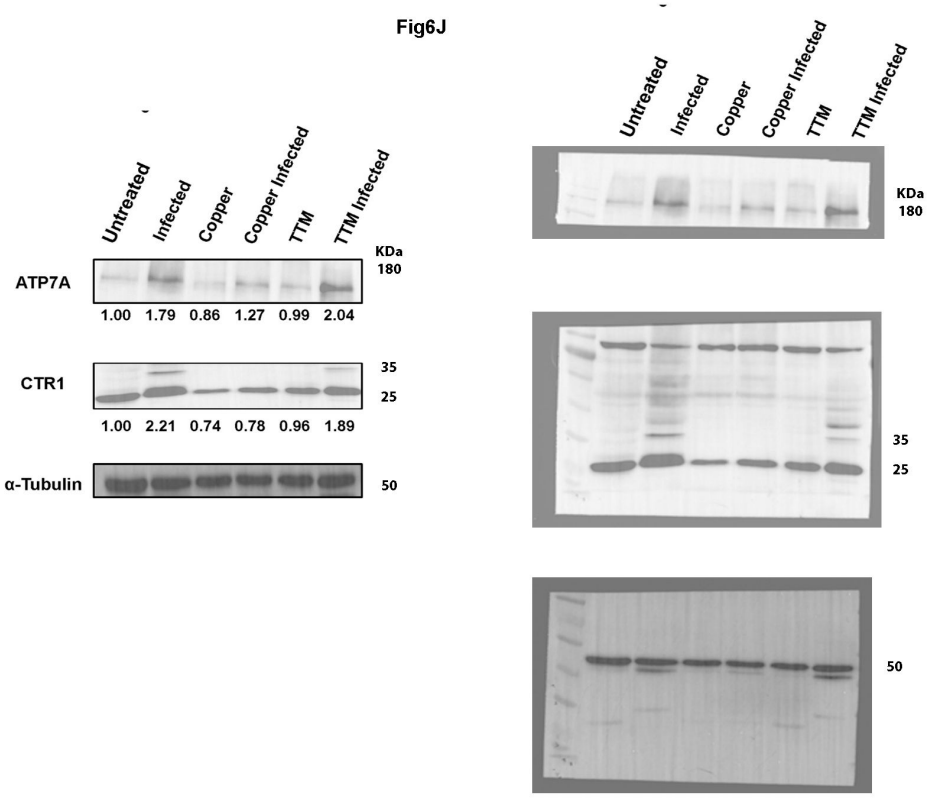


Fig6L

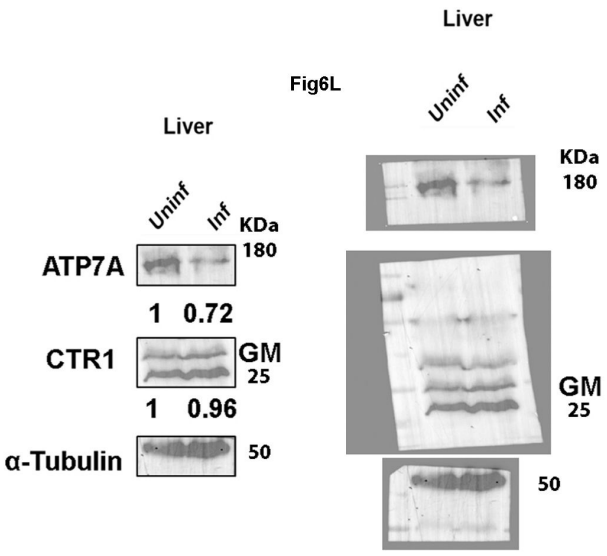
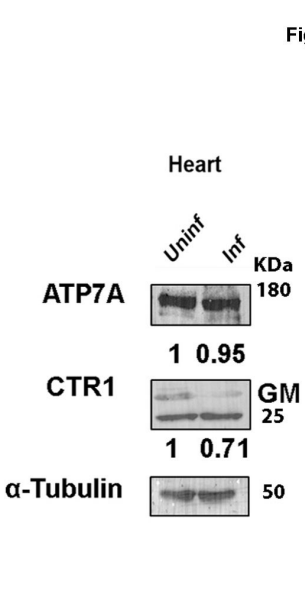
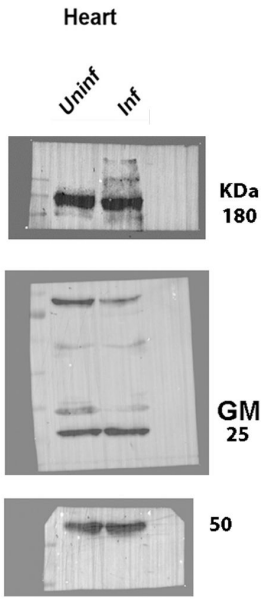
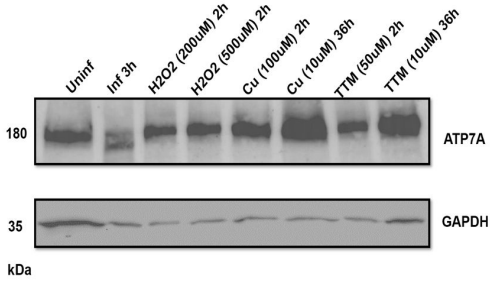


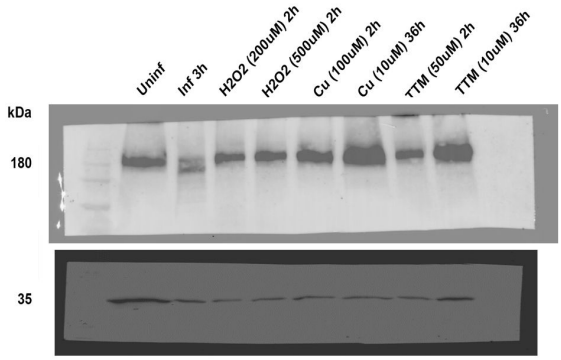
Fig6L



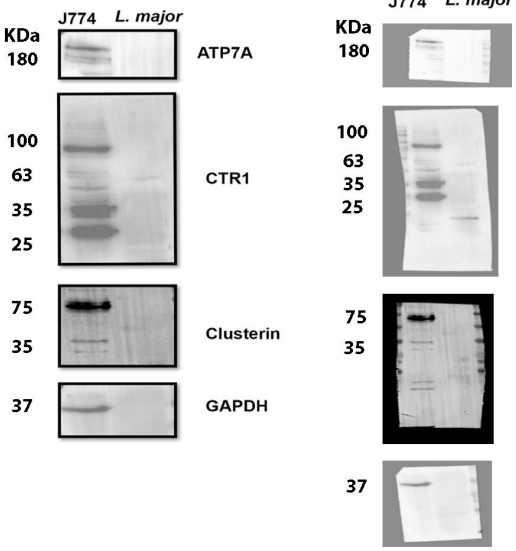


FigS2C

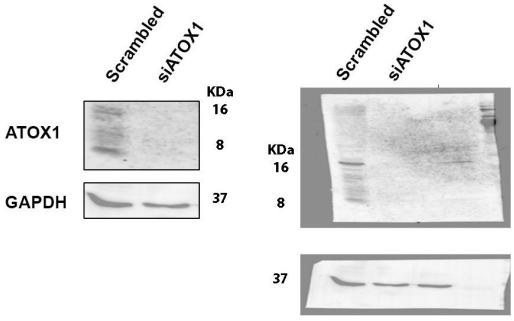




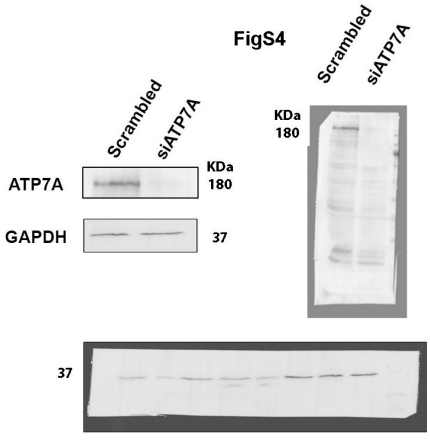
FigS3

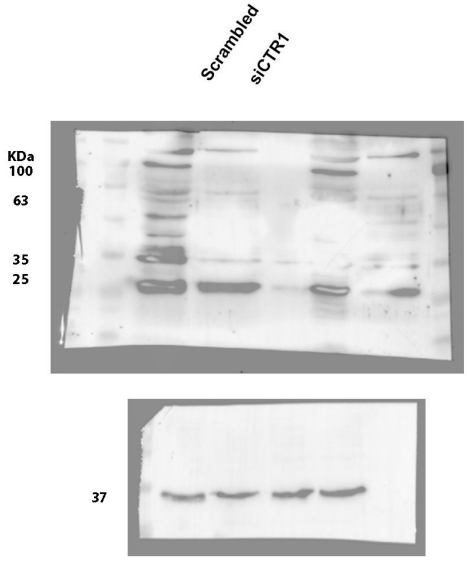


FigS4

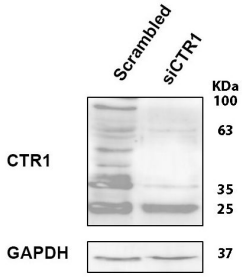


FigS4

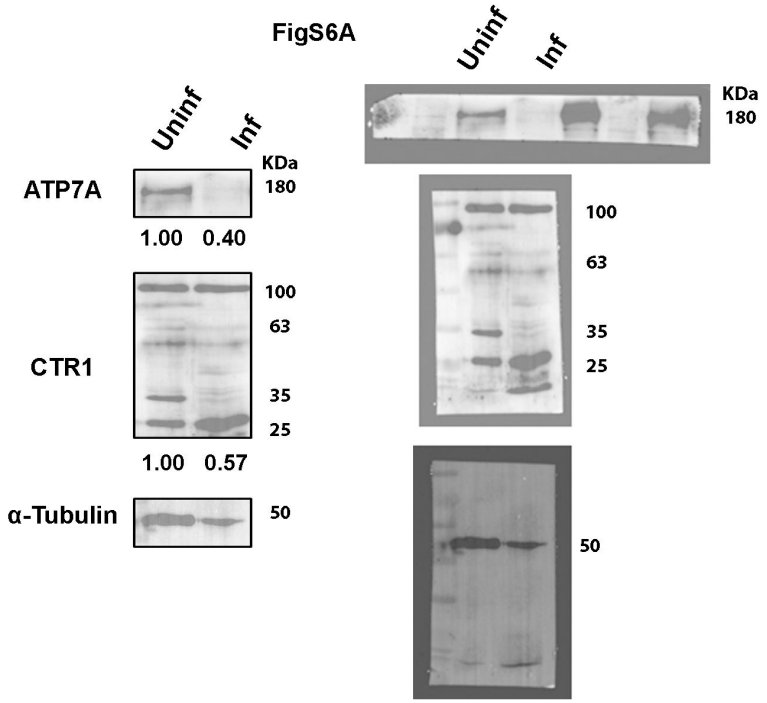


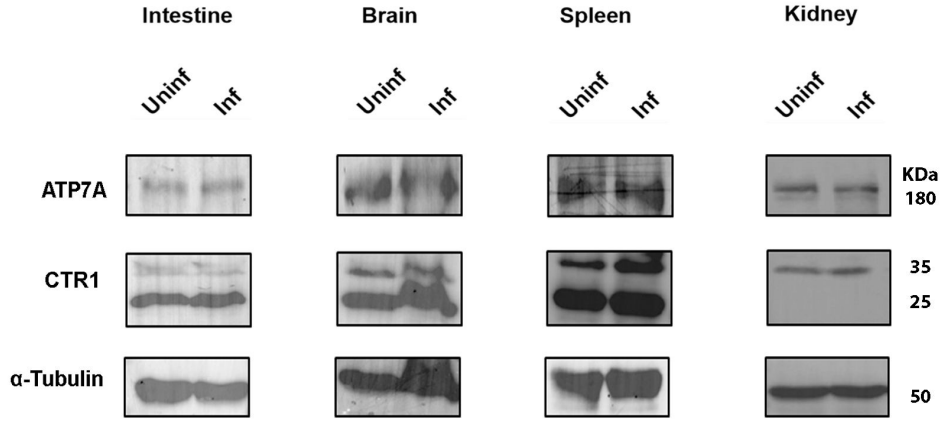


FigS4

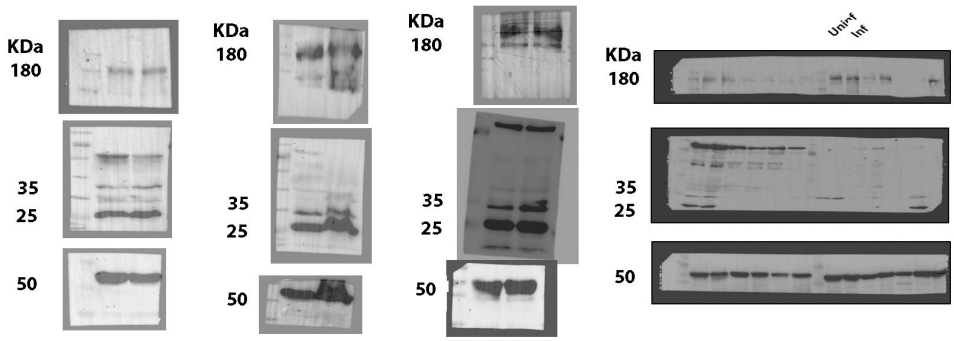


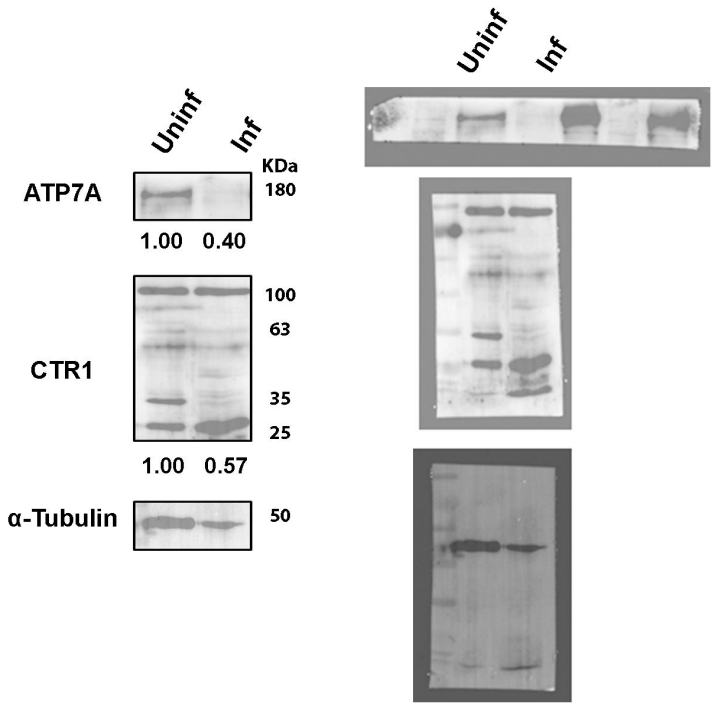
FigS6A

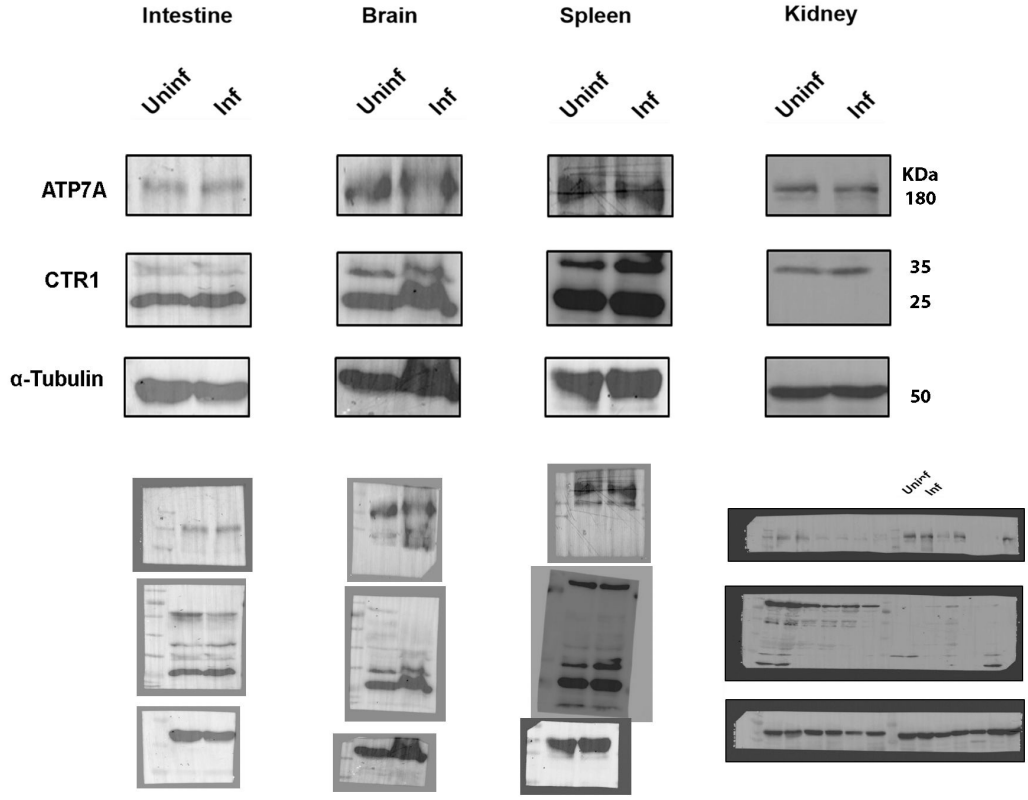




FigS6E




Uninf
Inf
ATP7A
KDa
180
1.00 0.40
CTR1
100
63
35
25
1.00 0.57
α-Tubulin
50


Intestine
Brain
Spleen
Kidney
Uninf
Inf
ATP7A
CTR1
α-Tubulin
KDa
180
35
25
50

Supplementary figures

Figure S1.

(A) Representative immunofluorescence image of ATP7A (green), co-stained with Golgi marker GM130 (magenta), in J774A.1 macrophages with no treatment , high copper (100 μM Cu) and copper chelated conditions (25 μM TTM) treatment for 2 hours. The merged images represent colocalization of ATP7A with GM130. The scale bar represents 5 μm. (B)) Fraction of ATP7A colocalization with GM130 from the above mentioned conditions is plotted. Asterisks indicate values that are significantly different from Basal samples. Sample size of macrophage (n): 13. $****p \leq 0.0001$, ns; (Wilcoxon rank-sum test).

Figure S2. Determination of parasite load and copper content of macrophage upon *Leishmania* infection and *Leishmania*-specific modulation of host ATP7A

(A) *Leishmania* load was determined by C_t values of *L.major* kDNA at indicated time points after infection of J774A.1 macrophages and normalised against 3 hour infection. Error bars represent mean ± SD of values calculated from three independent experiments. Asterisks indicate values that are significantly different from 3hr Infection samples. $**p \leq 0.01$, $***p \leq 0.001$, ns; (Student's t test). (B) Measurement of intracellular copper level using ICP-MS at the above mentioned condtions. Error bars represent mean ± SD of values calculated from three independent experiments. Asterisks indicate values that are significantly different from Uninfected samples. $*p \leq 0.05$, $**p \leq 0.01$, ns; (Student's t test). (C) Immunoblot of ATP7A of J774A.1 macrophages with and without 3 hour infection and indicated treatment conditions. GAPDH is used as housekeeping control.

Figure S3. No crossreactivity of host specific antibodies with *Leishmania* proteins

Immunoblot of ATP7A, CTR1, Clusterin and GAPDH from J774A.1 and *L. major* probed using host specific antibodies, representing lack of crossreactivity of host specific antibodies with *Leishmania* proteins.

Figure S4. Confirmation of knockdown of host copper regulators via siRNA

Immunoblots of ATP7A, CTR1 and ATOX1 after treatment of J774A.1 macrophages with scrambled siRNA and ATP7A, CTR1 or ATOX1 siRNA respectively, confirming siRNA-mediated knockdowns. GAPDH is used as housekeeping control.

Fig S5. CTR1 endocytosis is not triggered by latex phagocytic beads

Immunofluorescence image of CTR1 (green) in J774A.1 macrophage with FluoSpheres™ Carboxylate-modified Microsphere beads (magenta) confirming absence of endocytosis of CTR1 due to general phagoscytosis triggered by the beads. Macrophage nuclei is stained with DAPI (blue).

Fig S6. ATP7A and CTR1 of peritoneal macrophages are modulated by *L.major* infection. Optimal treatment of copper and TTM changes mice copper content without side effects, while *Leishmania* infection does not alter expression copper regulators in intestine, brain, spleen and kidney

(A) Immunoblot of ATP7A and CTR1 from thioglycollate elicited peritoneal macrophages from BALB/c mice with or without *L.major* infection for 3 hours. The fold changes of ATP7A and CTR1 glycosylated monomer abundance normalized against housekeeping control α-tubulin have been mentioned. Measurement of (B) whole serum copper of BALB/c mice, (C) Ceruloplasmin level representative of serum bioavailable copper, normalised to that of the untreated mice and (D) Haemoglobin levels, 4 weeks post initiation of respective treatments to simulate different copper conditions. Error bars represent mean ± SD of values. Asterisks indicate values that are significantly different from Untreated samples. Sample size (n): 6 for each condition, $*p \leq 0.05$, $***p \leq 0.001$, ns; (Student's t test). (E) Immunoblot of ATP7A and CTR1 from intestine, brain, spleen and kidney of infected and uninfected mice. The fold changes of ATP7A and CTR1 glycosylated monomer abundance normalized against housekeeping control α-tubulin have been mentioned.

Fig S7. Uncropped blots

Uncropped blots are indicated to their corresponding figures. The same GAPDH loading control was used for the infected samples in Fiure 2G and Figure 2F. GAPDH loading control is same for Figure 2A and 4E where same conditions were used to check the protein levels of ATP7A and CTR1.

Table S1. Oligonucleotides used in this paper

Primer	Primer Sequence (5'- 3')
ATP7AFP	GAAGAGGTCGGACTGCTGTC
ATP7ARP	CCTTAGTAATGCCAACCTGAGAAGC
CTR1FP	CAAGATAGCCCGAGAGGGTC
CTR1RP	GATGTGCAGCACTGTCTGC
COMMD1FP	CAAGATAGCCCGAGAGGGTC
COMMD1RP	GATGTGCAGCACTGTCTGC
ClusterinFP	AGGAAAAGCCGTGCGGAAT
ClusterinBP	GCCTGGAGACATGTGGAGTT
mGAPDHFP	CGTGCCTGGAGAAACC
mGAPDHRP	TGGAAGAGTGGGAGTTGCTGTTG
kDNA_FP	AAGGGTGAACGCCAAAAACG
kDNA_RP	GTTCGGTTAATCCGCGAACG

Table S2.

Antibody Name	Type	Catalog Number
Rabbit Anti-ATP7A antibody	Primary	Abcam ab13995
Rabbit Anti-CTR1 antibody	Primary	Abcam ab129067
Rabbit Anti-COMMD1 antibody	Primary	Abcam ab102794
Rabbit Anti Clusterin Beta Chain antibody	Primary	Abcam ab184099
Rabbit Anti-GAPDH antibody	Primary	BioBharati BB-AB0060
Mouse Anti-Lamp1 antibody	Primary	DSHB H4A3
Mouse Anti-alpha 1 Sodium Potassium ATPase antibody	Primary	Abcam ab7671
Rabbit Anti-Tubulin alpha antibody	Primary	Affinity Biosciences AF7010
Anti-rabbit IgG, HRP-linked Antibody	Secondary	CST#7074
Anti-mouse IgG, HRP-linked Antibody	Secondary	CST#7076
Donkey Anti-Rabbit Alexa488	Secondary	Life Technologies A-21206
Donkey Anti-Mouse Alexa568	Secondary	Life Technologies A-11057