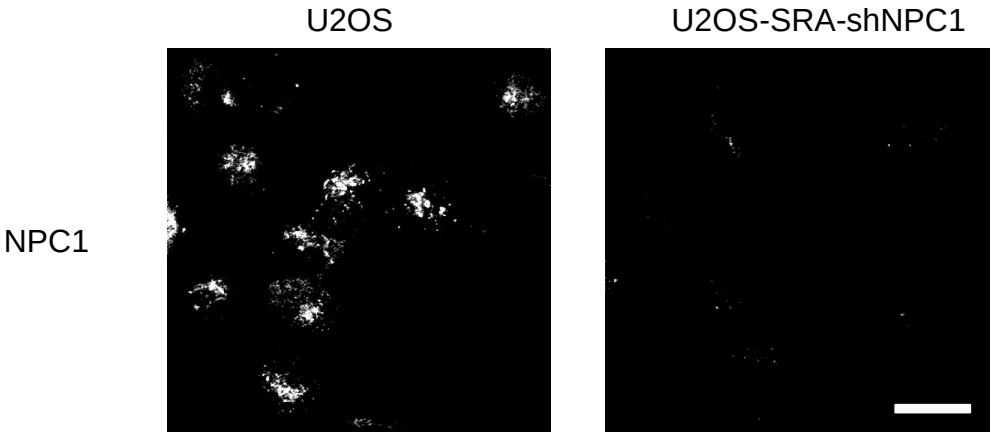
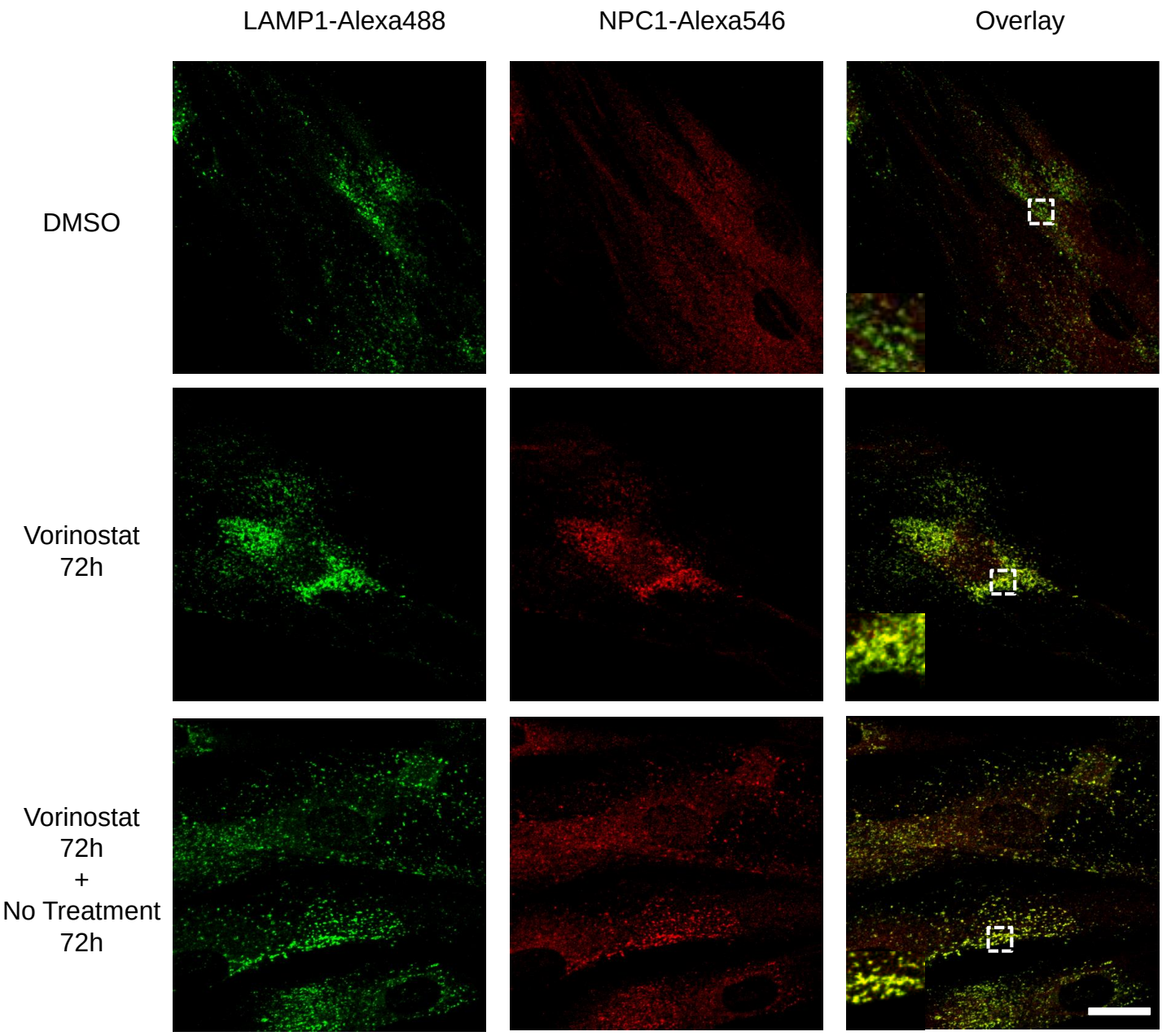
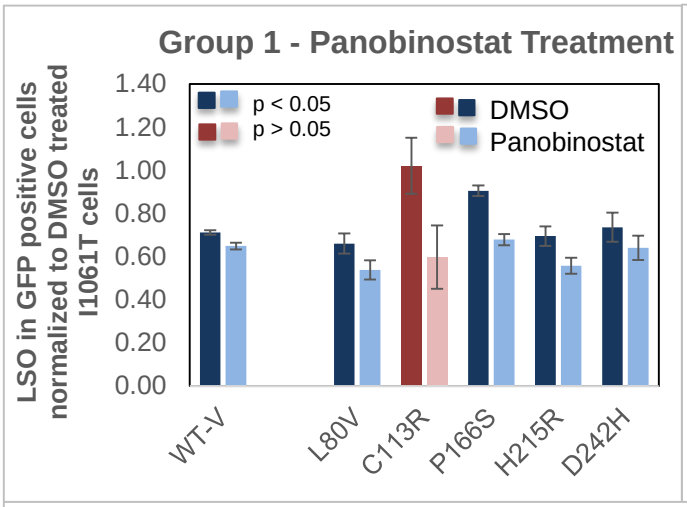
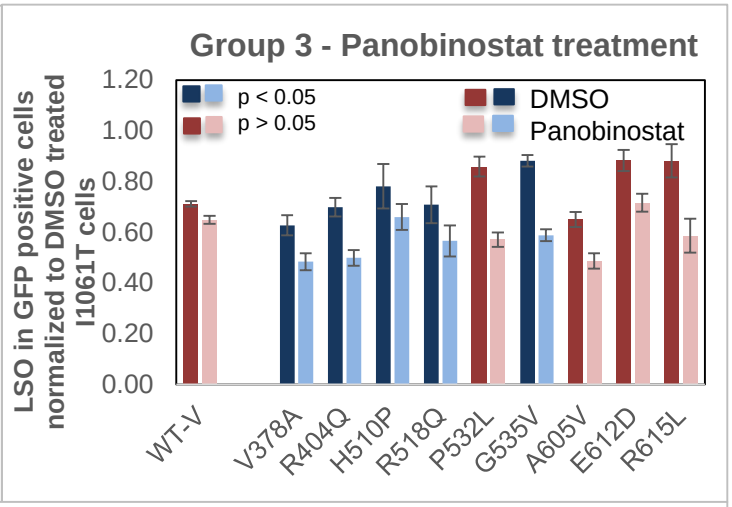


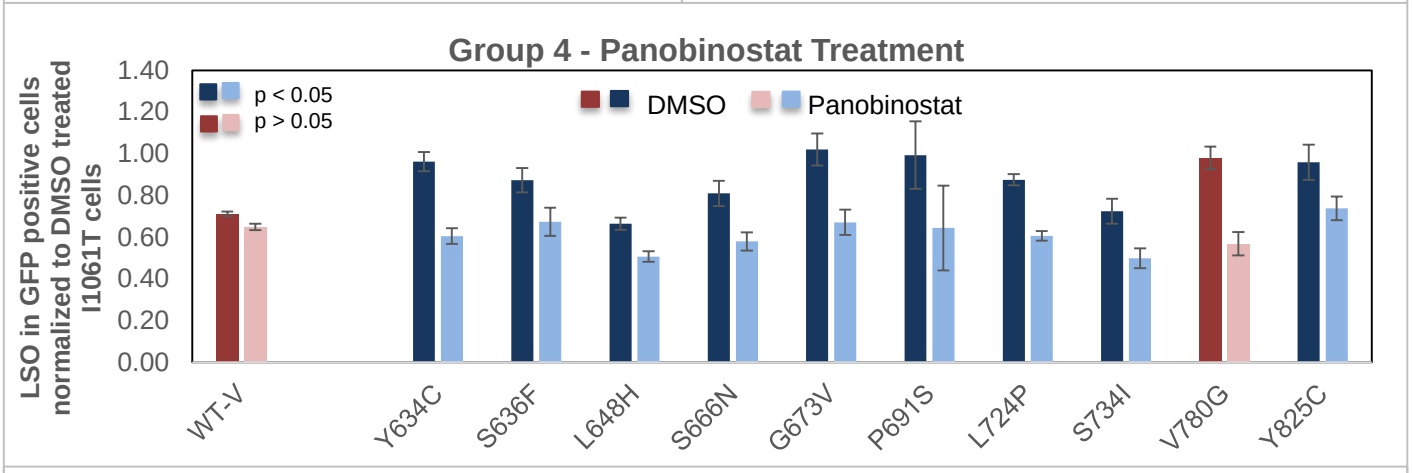
Supplemental Figure S1. **Testing specificity of rabbit polyclonal anti-hNPC1 antibody:** U2OS (WT) and U2OS-SRA-shNPC1 cells were plated in poly-D-lysine coated cover-slip bottom dishes. Two days after plating, cells were fixed with 2% PFA permeabilized and immunostained with a primary rabbit anti-NPC1 antibody and counter-stained with goat anti rabbit Alexa546 secondary antibody. Images were acquired on Zeiss LSM880 confocal microscope using a 63X objective. Images shown are sum projections. . Scale bar = 10 µm.

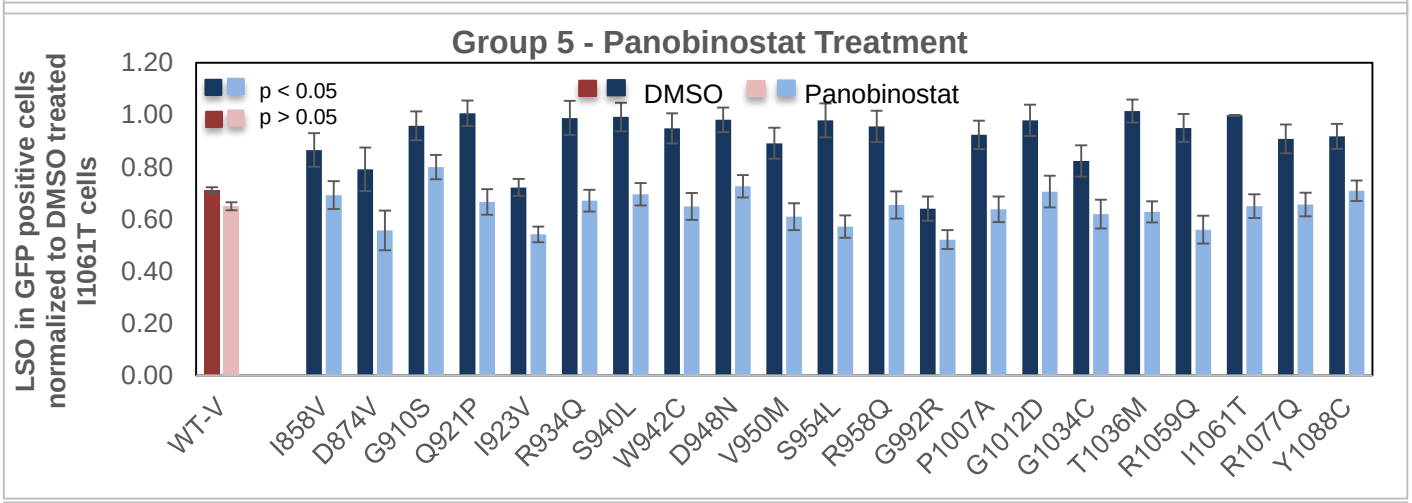


Supplemental Figure S2: Co-localization of NPC1 with LAMP1 in NPC1 mutant fibroblasts.
GM18453 cells were plated in poly-D-lysine coated cover-slip bottom dishes in MEM growth medium supplemented with 5.5% FBS. On day 2 cells were treated with DMSO or 10µM Vorinostat and incubated for 72 hours. After 72 hours, Vorinostat supplemented media was replaced with growth medium without Vorinostat and incubated for additional 72 hours. Cells were finally fixed with 2% PFA, permeabilized and immunostained for NPC1 (rabbit anti-hNPC1) followed by goat anti rabbit Alexa 546 and LAMP1 (rabbit anti-LAMP1) followed by goat anti rabbit Alexa 488 secondary antibody respectively. Images were acquired on Zeiss LSM880 confocal microscope using a 63X objective. Images shown are average projections. The region outlined in the Overlay images is shown at higher magnification in the inset. Scale bar = 10 µm.


Group 1 - Panobinostat Treatment
LSO in GFP positive cells normalized to DMSO treated I1061T cells
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
p < 0.05
p > 0.05
DMSO
Panobinostat
WT-V
L80V
C113R
P166S
H215R
D242H


Group 3 - Panobinostat treatment
LSO in GFP positive cells normalized to DMSO treated I1061T cells
1.20
1.00
0.80
0.60
0.40
0.20
0.00
p < 0.05
p > 0.05
DMSO
Panobinostat
WT-V
V378A
R404Q
H510P
R518Q
P532L
G535V
A605V
E612D
R615L


Group 4 - Panobinostat Treatment
LSO in GFP positive cells normalized to DMSO treated I1061T cells
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
p < 0.05
p > 0.05
DMSO
Panobinostat
WT-V
Y634C
S636F
L648H
S666N
G673V
P691S
L724P
S734I
V780G
Y825C


Group 5 - Panobinostat Treatment
LSO in GFP positive cells normalized to DMSO treated I1061T cells
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1.00
0.80
0.60
0.40
0.20
0.00
p < 0.05
p > 0.05
DMSO
Panobinostat
WT-V
I858V
D874V
G910S
Q921P
I923V
R934Q
S940L
W942C
D948N
V950M
S954L
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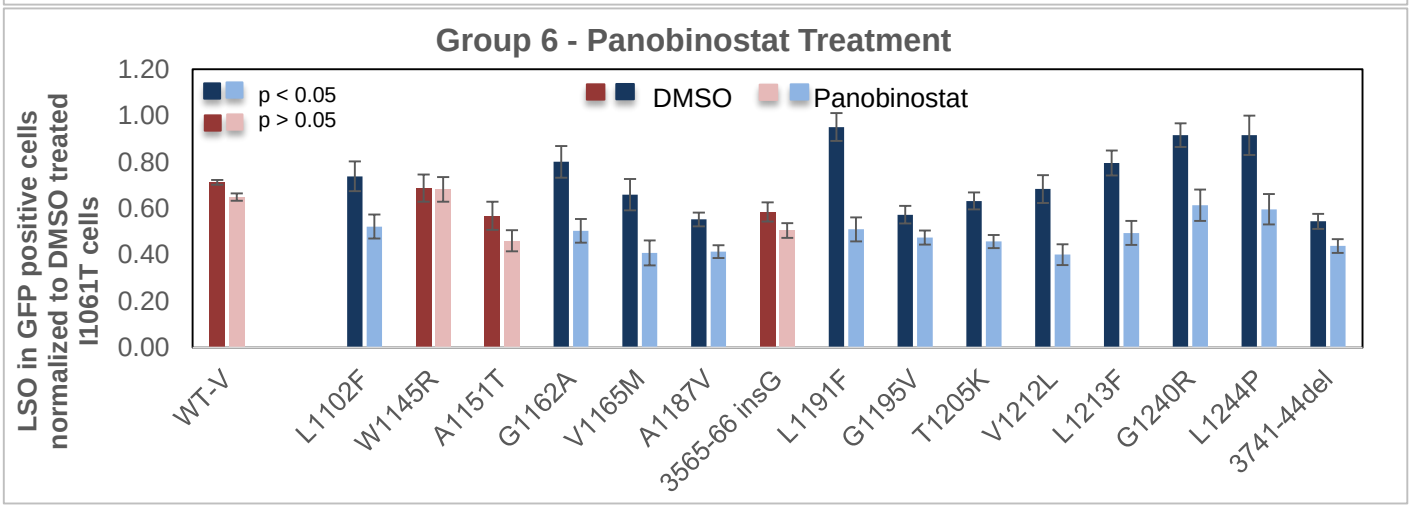
G1012D
G1034C
T1036M
R1059Q
I1061T
R1077Q
Y1088C


Group 6 - Panobinostat Treatment
LSO in GFP positive cells normalized to DMSO treated I1061T cells
1.20
1.00
0.80
0.60
0.40
0.20
0.00
p < 0.05
p > 0.05
DMSO
Panobinostat
WT-V
L1102F
W1145R
A1151T
G1162A
V1165M
A1187V
3565-66 insG
L1191F
G1195V
T1205K
V1212L
L1213F
G1240R
L1244P
3741-44del

Supplemental Figure S3. **Quantification of effects of Panobinostat on cholesterol accumulation in NPC1 mutants.**
The effect of 50 nM Panobinostat was tested on 60 different NPC1 mutations from five segments of the NPC1 protein as illustrated in Figure 8. DMSO was used as a solvent control. Filipin fluorescence images of the transfected cells were analyzed to obtain an LSO value as explained in methods. Data represent averages ± SEM from 15-25 images. Each image includes about 1-5 transfected cells. Dark blue (DMSO treated) and light blue bars (Panobinostat treated) for each group represent mutants that showed reduction in LSO values with $p<0.05$, and dark red (DMSO treated) and pink bars (Panobinostat treated) represent mutants that showed no significant reduction in LSO value. Statistical significance was measured by t-test with two-tailed distribution and two-sample equal variance (homoscedastic) type using Microsoft Excel software.