Supplementary Figure Legends

Figure. S1. Illustrations on calculating perinuclear lysosomal index in STHdhQ7 and SThdhQ111 cells. Detailed procedure is described in the method section. Nuclear region (N) was first outlined based on DAPI staining. The nuclear outline was then expanded by 2 μm as the perinuclear region (PN). Finally, the image was adjusted to overexposure and the cellular boundary is outlined based on Lamp1 staining (C).

Figure S2. Staining of lysosomes in live STHdhQ7 and STHdhQ111 cells with LysoTracker DND-99. Cells were grown on 35mm glass bottom dishes. 50 nM LysoTracker DND-99 and 5 μg/ml DAPI were added to the cells and incubated for 30 min. After incubation, cells were briefly washed with complete medium to remove the free dye and incubated in complete medium. Images were directly taken with a Zeiss LSM700 confocal microscopy at the room temperature. The cell boundary is outlined.

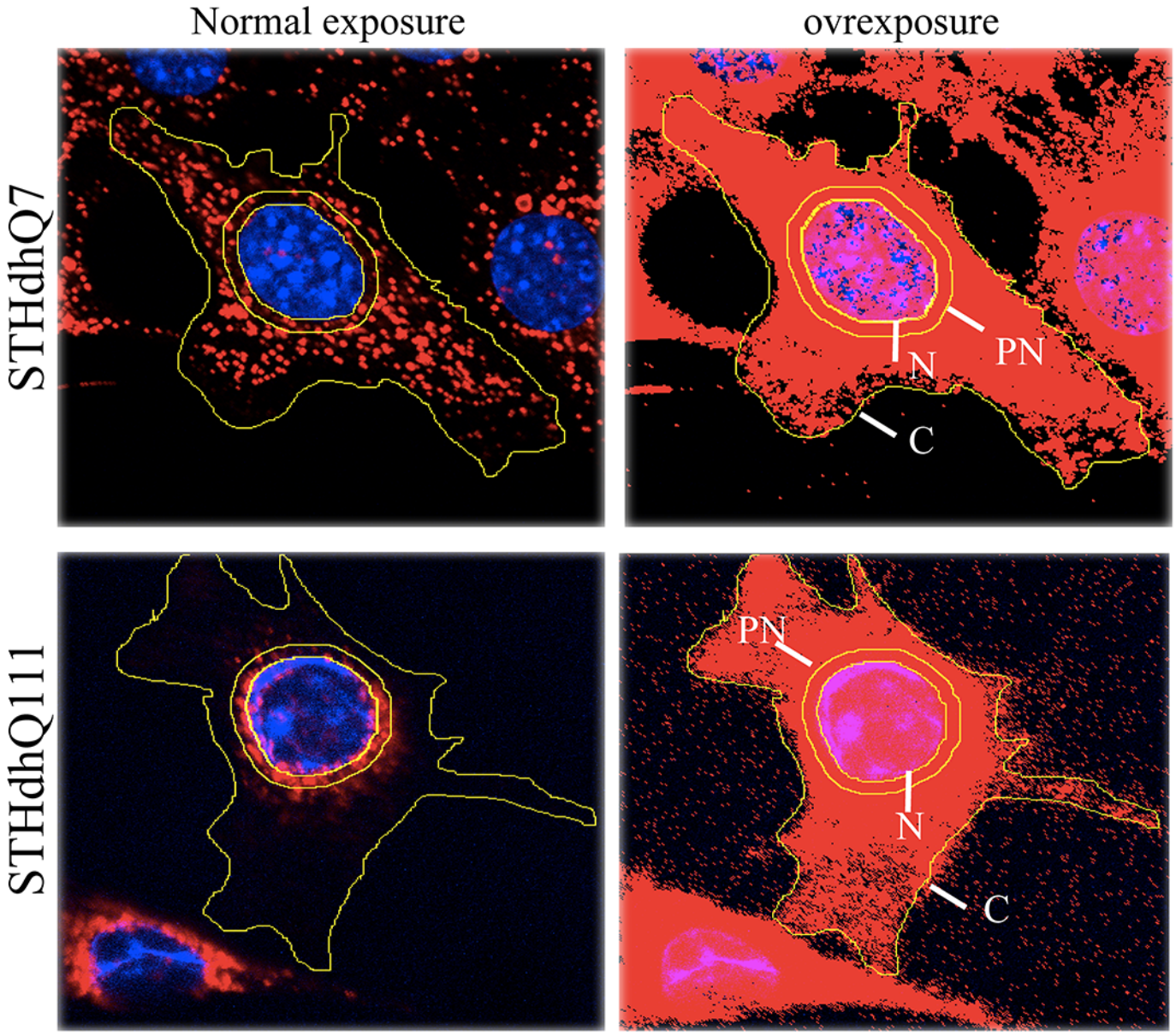
Figure S3. Confocal images from representative LysoTracker Red DND-99 FRAP experimental time course in STHdhQ7 cells. The green bar indicates the time of photo bleach and the box outlines the photo bleached area (11.88 μm x 11.46 μm). Total image size 34.38 μm x 40.84 μm.

Figure S4. Confocal images from representative LysoTracker Red DND-99 FRAP experimental time course in STHdhQ111 cells. The green bar indicates the time of photo bleach and the box outlines the photo bleached area (11.25 μm x 10.21μm). Total image size 35.22 μm x 38.55 μm.

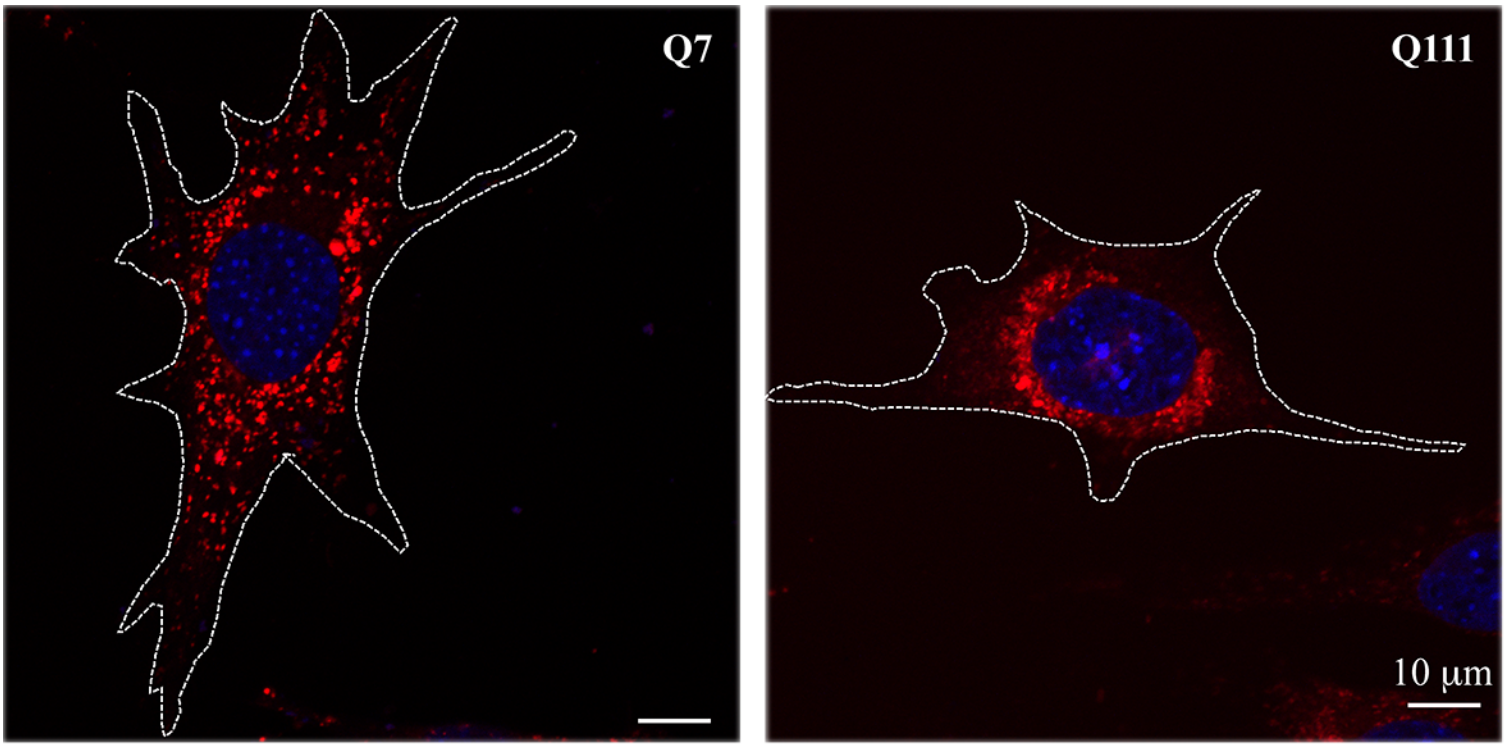
Figure S5. A representative confocal image of Lamp1 staining in STHdhQ7 cells over-expressing fHtt145Q-EGFP. Note that fHtt145Q-EGFP forms perinuclear aggregated as indicated by the arrow.

Figure S6. Immunofluorescent studies of the co-localization of Htt and Lamp1 in STHdhQ7 and STHdhQ111 cells. STHdh cells were fixed in 4% PFA and co-stained with anti-Htt (MAB#2166,

against amino acids 181-810, Millipore, MA, USA) and anti-Lamp1. **A-B.** Representative images showing the co-localization of Htt and Lamp1 in STHdhQ7 (A) and STHdhQ111 (B) cells. **A1-B1.** Line scans of fluorescence intensities of Htt and Lamp1 through the white line shown in A and B respectively. **C.** Correlation co-efficiency analysis for co-localization of Htt and Lamp1 in STHdh cells. The co-localization analysis was performed using ImageJ software. Background was first subtracted from each channel using ImageJ. Manders' coefficient was calculated with the Intensity Correlation Analysis plug-in. The whole cell image was designated as the ROI (region of interest) during the analysis.

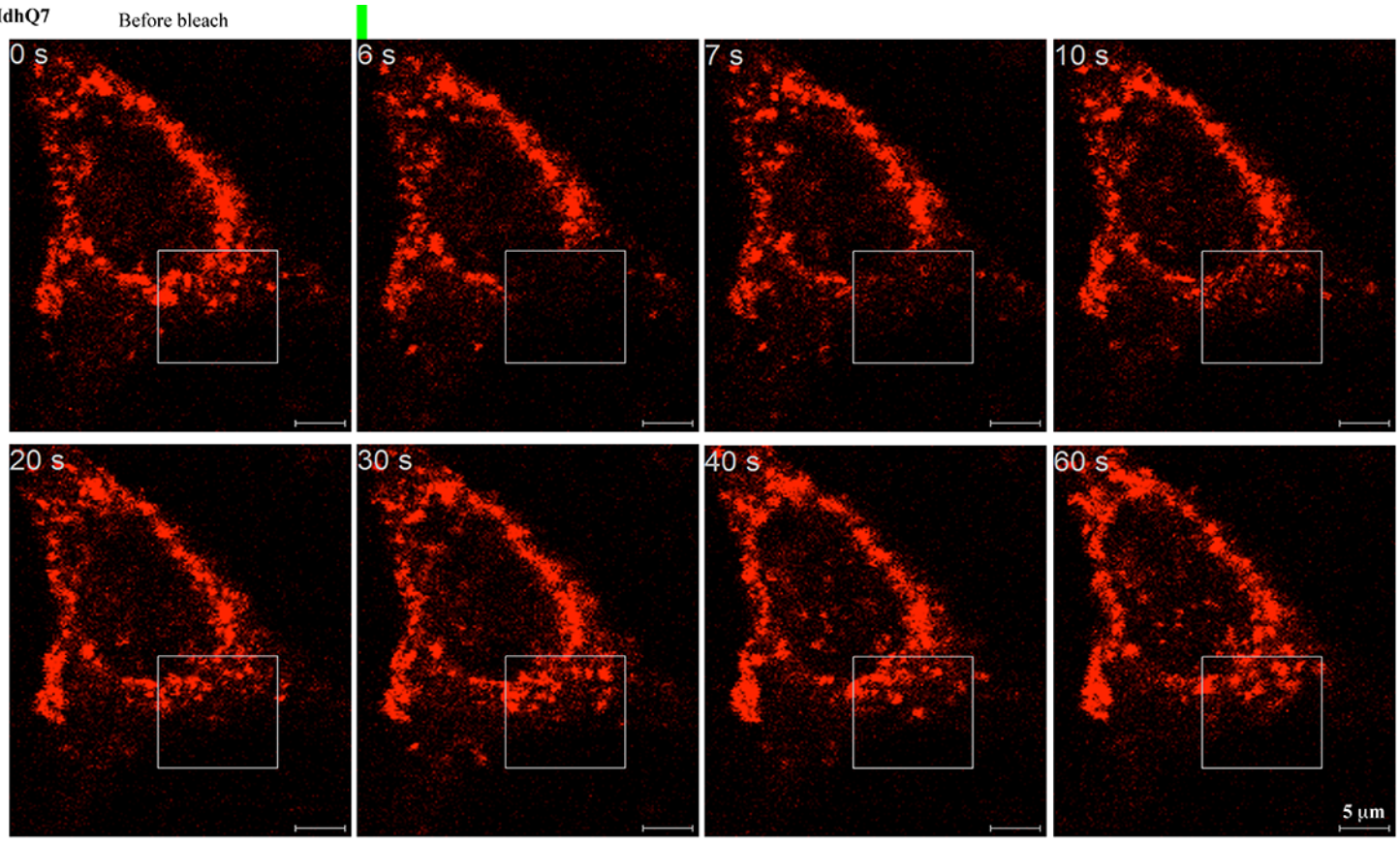


Supplementary Fig. S1

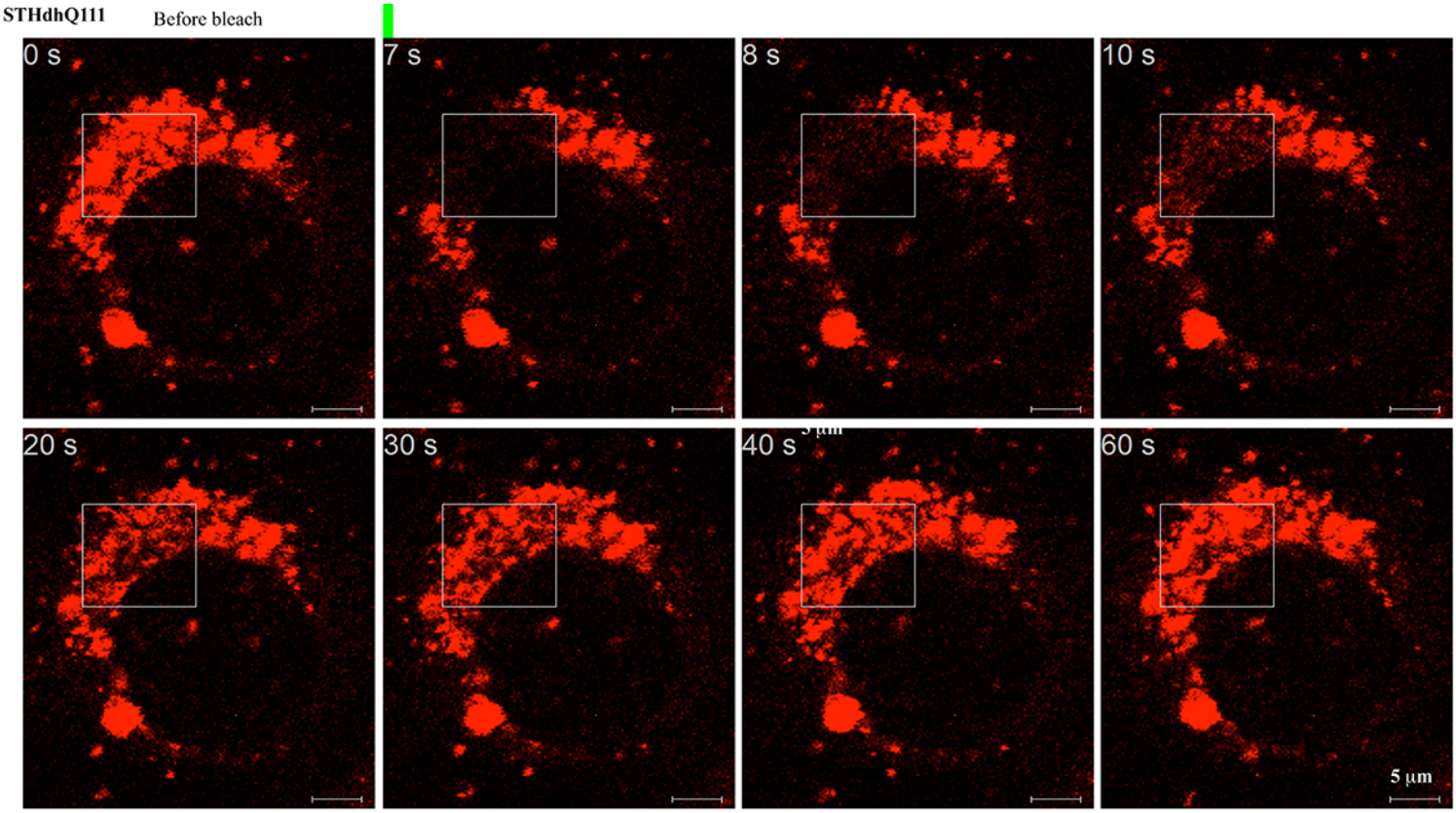


DAPI/Lysotracker DND-99

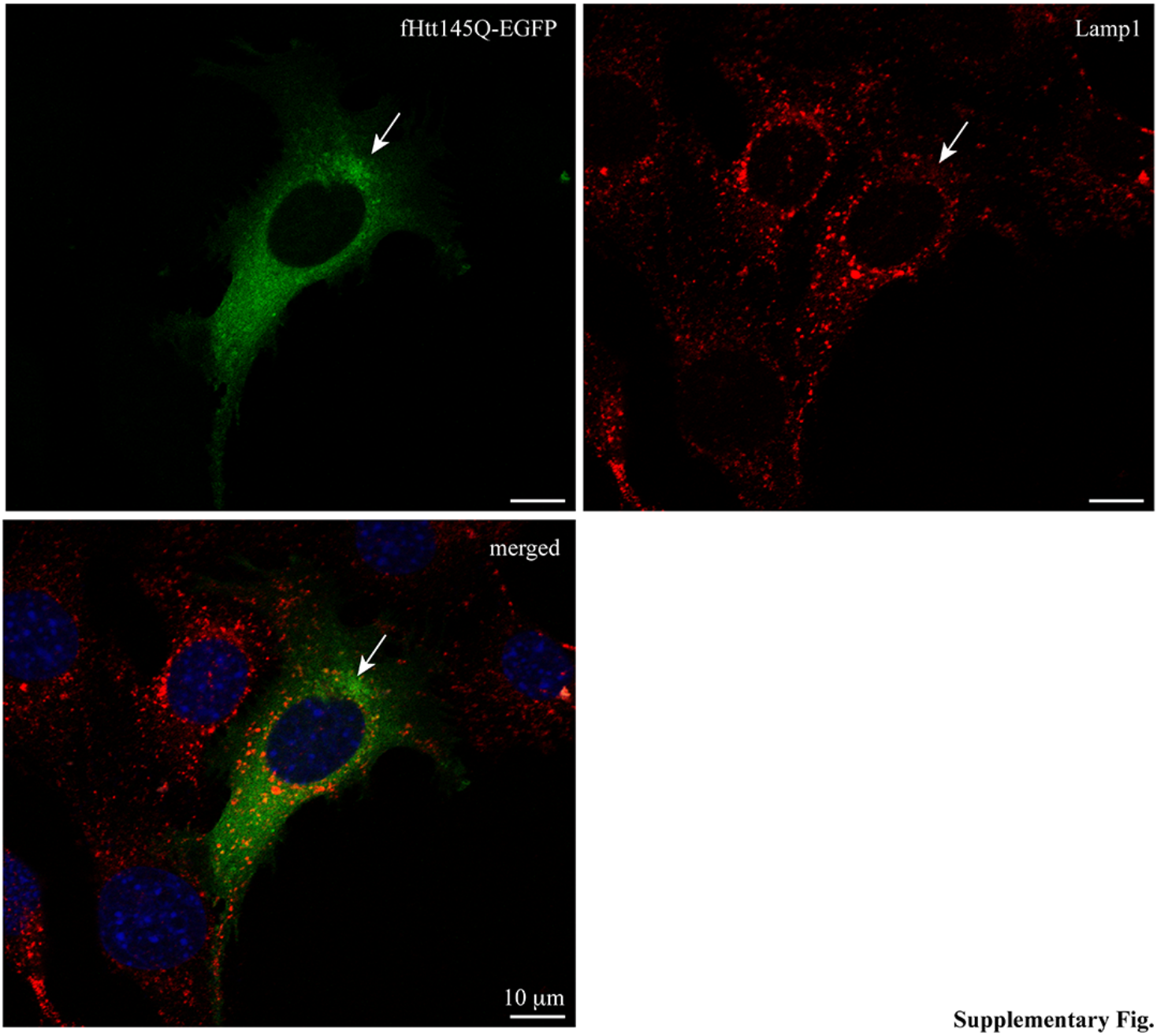
Supplementary Fig. S2



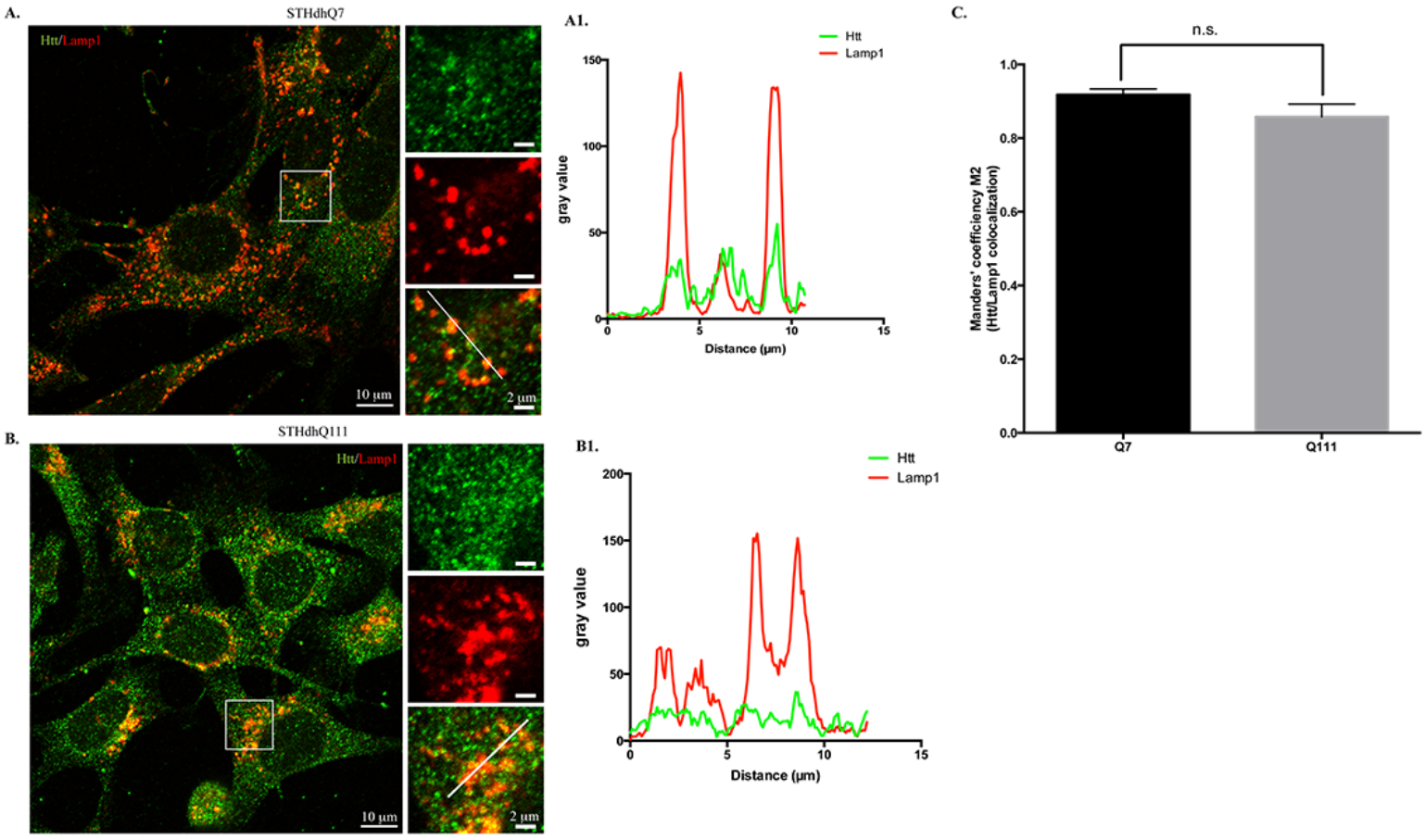
Supplementary Fig. S3



Supplementary Fig. S4



Supplementary Fig. S5



Supplementary Fig. S6