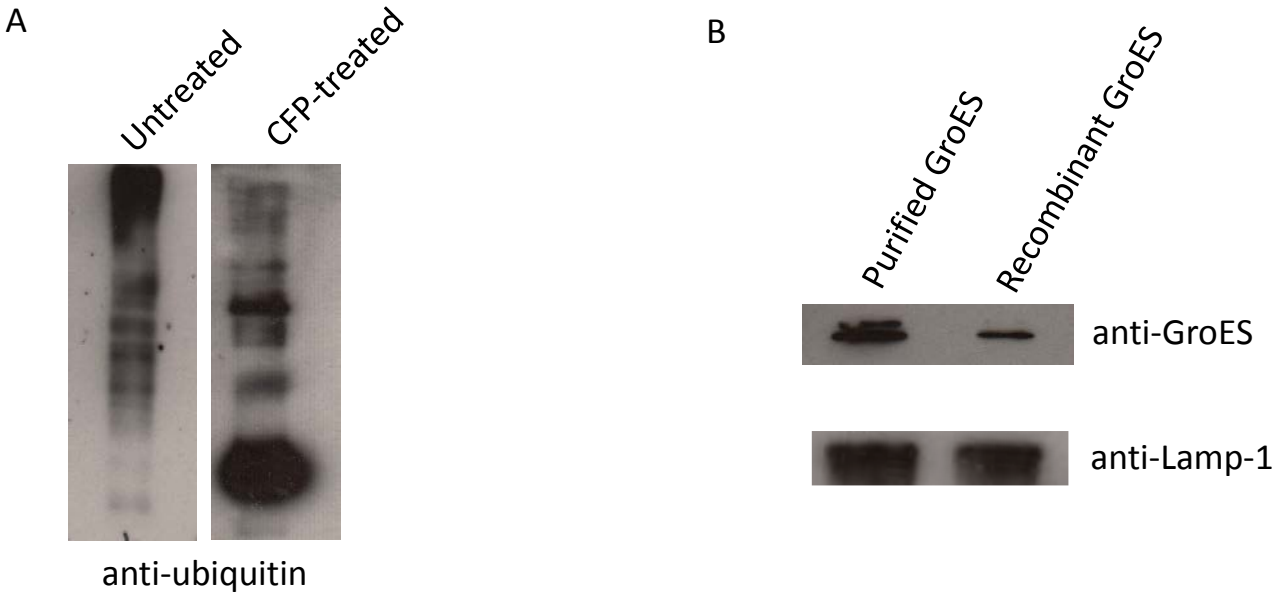
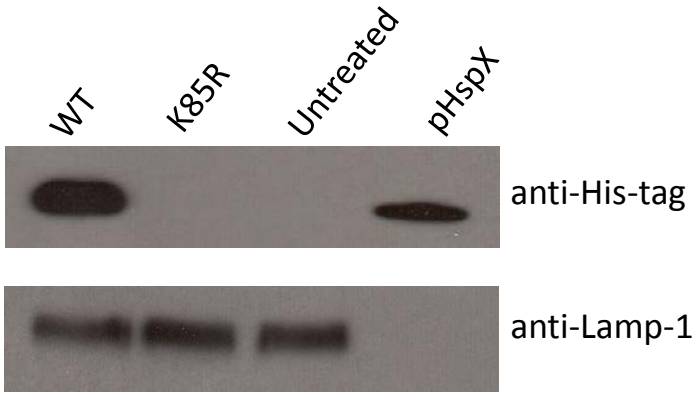
Supplementary Figure 1



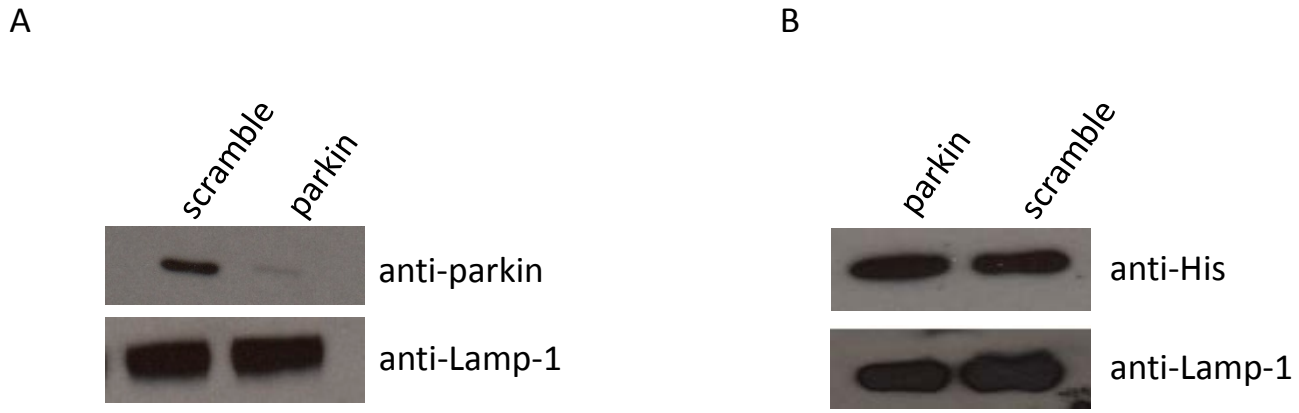
Supplementary figure 1: **(A)** Raw 264.7 cells were pulsed with *M.tb* culture filtrate proteins (CFP) or left untreated for 16 hours. Following treatment, exosomes were purified from cell culture supernatant. Exosomes from uninfected and CFP-pulsed macrophages (10μg) were probed for the presence of mono-ubiquitin by western blot. **(B)** Raw 264.7 cells were pulsed for 16 hours with purified GroES or recombinant GroES with the His-tag removed by endopeptidase digestion. Exosomes were purified from cell culture supernatant and probed for the presence of GroES. Loading control; Lamp-1.

Supplementary Figure 2



Supplementary figure 2: Raw 267.4 cells were left untreated or infected with *M. smegmatis* expressing wild-type *M.tb* HspX, or K85R *M.tb* HspX for 72 hours. Exosomes were purified from the cell culture supernatant by ultracentrifugation followed by flotation on a sucrose gradient. Purified exosomes (10µg)) were assayed for presence of the wild-type and mutant His-HspX proteins by western blot using a polyclonal His-tag antibody. Lamp-1 was used as a loading control. pHspX; purified HspX from *E. coli* (positive control).

Supplementary figure 3:



Supplementary figure 3: The ubiquitin ligase parkin is not responsible for the HspX ubiquitination. **(A)** Raw 264.7 cells were treated for 24 hours with the siRNA directed against parkin and the cell lysates of treated cells were analyzed for parkin protein expression by western blot. Scrambled siRNAs were used as a control. **(B)** Raw264.7 cells treated with the siRNA for parkin or the scrambled siRNA were pulsed with His-HspX protein for 16 hours. Exosomes were isolated from cell culture supernatant and the purified exosomes (10ug) were probed for the presence of His-tagged HspX by western blot.

Supplementary Table 1: List of E3 Ligases associated with endosomal compartments with references

E3 Ligase	Reference
Carp-2	Liao, W. et al. CARP-2 Is an Endosome-Associated Ubiquitin Ligase for RIP and Regulates TNF-Induced NF-κB Activation. Curr. Biol. 18, 641–649 (2008).
Nedd4-1	Sugeno, N. et al. Lys-63-linked ubiquitination by E3 ubiquitin ligase Nedd4-1 facilitates endosomal sequestration of internalized α-synuclein. J. Biol. Chem. 289, 18137–51 (2014).
NKLAM	Lawrence, D. W. & Kornbluth, J. E3 ubiquitin ligase NKLAM is a macrophage phagosome protein and plays a role in bacterial killing. Cell. Immunol. 279, 46–52 (2012).
RFP13	Bocock, J. P., Carmicle, S., Madamba, E. & Erickson, A. H. Nuclear targeting of an endosomal E3 ubiquitin ligase. Traffic 11, 756–66 (2010).
Itchy	Carayon, K. et al. Proteolipidic composition of exosomes changes during reticulocyte maturation. J. Biol. Chem. 286, 34426–34439 (2011).
Ring Finger 40	unpublished, ExoCara.org database
Nedd4L	Mathivanan, S. et al. Proteomics analysis of A33 immunoaffinity-purified exosomes released from the human colon tumor cell line LIM1215 reveals a tissue-specific protein signature. Mol. Cell. Proteomics 9, 197–208 (2010).
Mahogunin ring finger 1	Gonzales, P. a et al. Large-scale proteomics and phosphoproteomics of urinary exosomes. J. Am. Soc. Nephrol. 20, 363–79 (2009).
HUWE1	Gonzales, P. a et al. Large-scale proteomics and phosphoproteomics of urinary exosomes. J. Am. Soc. Nephrol. 20, 363–79 (2009).
Uhr4	Carayon, K. et al. Proteolipidic composition of exosomes changes during reticulocyte maturation. J. Biol. Chem. 286, 34426–34439 (2011).
wwp1	Carayon, K. et al. Proteolipidic composition of exosomes changes during reticulocyte maturation. J. Biol. Chem. 286, 34426–34439 (2011).
Ube3c	unpublished, ExoCara.org database
wwp2	Carayon, K. et al. Proteolipidic composition of exosomes changes during reticulocyte maturation. J. Biol. Chem. 286, 34426–34439 (2011).
Herc5	Gonzales, P. a et al. Large-scale proteomics and phosphoproteomics of urinary exosomes. J. Am. Soc. Nephrol. 20, 363–79 (2009).
SMURF1	Gonzales, P. a et al. Large-scale proteomics and phosphoproteomics of urinary exosomes. J. Am. Soc. Nephrol. 20, 363–79 (2009).