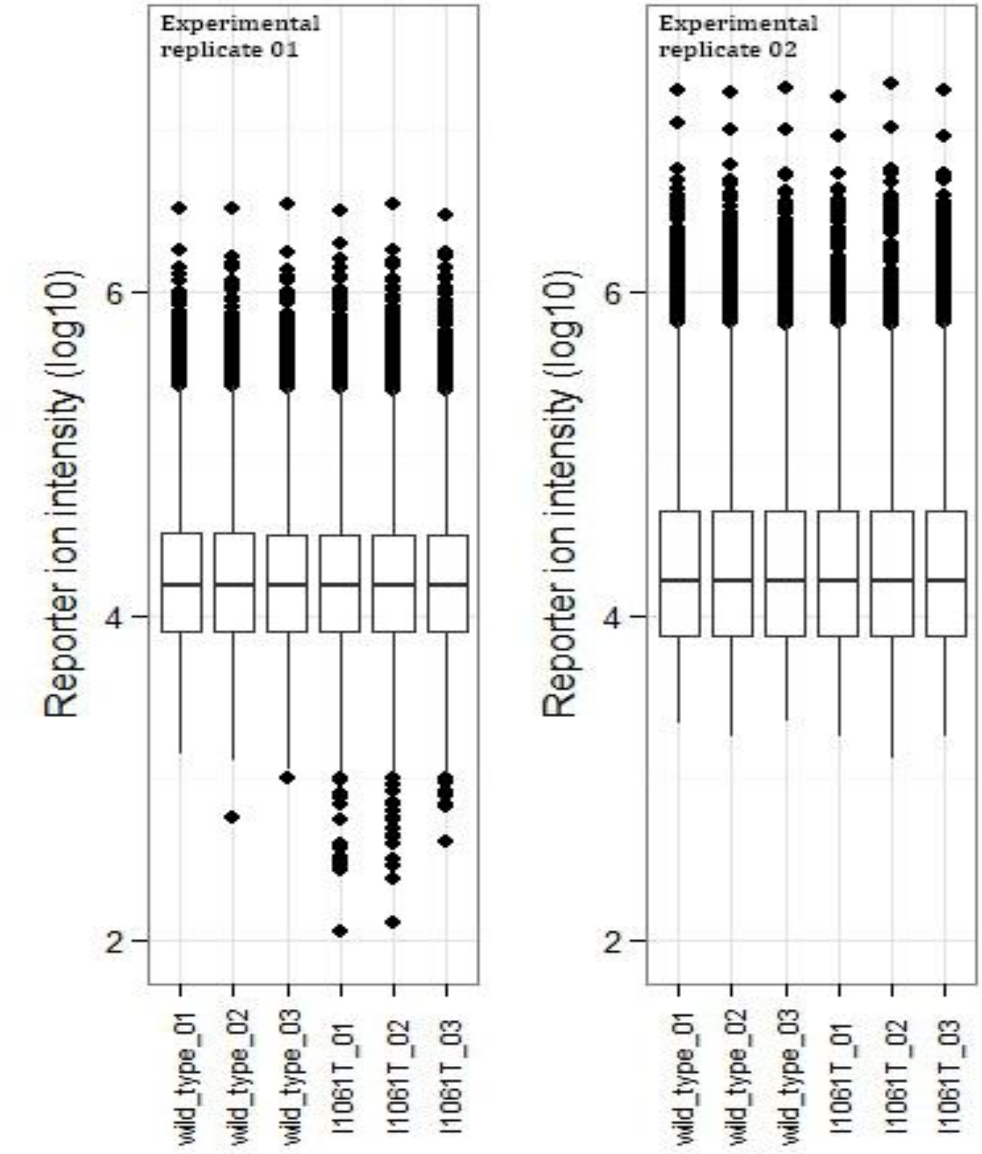
Figure Legends (Supplementary Figures)

Figure S1(a). Box plots of the normalized $\log_{10}$ of the reporter ion intensities of each TMT isobaric mass tags in the two experimental replicates. For each box plot, the median value is represented by the central, horizontal line. **(b)** Scatter plot showing the number of peptides and spectra match per protein in experimental replicate-02. **(c)** Number of quantified proteins and the corresponding number of MS/MS spectra used to compute expression ratios ($\mathrm{NPC1I}^{1061\mathrm{T}}/\mathrm{NPC1}^{\mathrm{WT}}$). For example, 860 proteins were quantified by a single spectrum in experimental replicate-01 and 800 proteins in replicate-02, respectively. **(d)** Median absolute deviation (MAD) of the quantified proteins from replicate-01 and 02.

Figure S2. DEPs observed in only one of the experimental replicates.

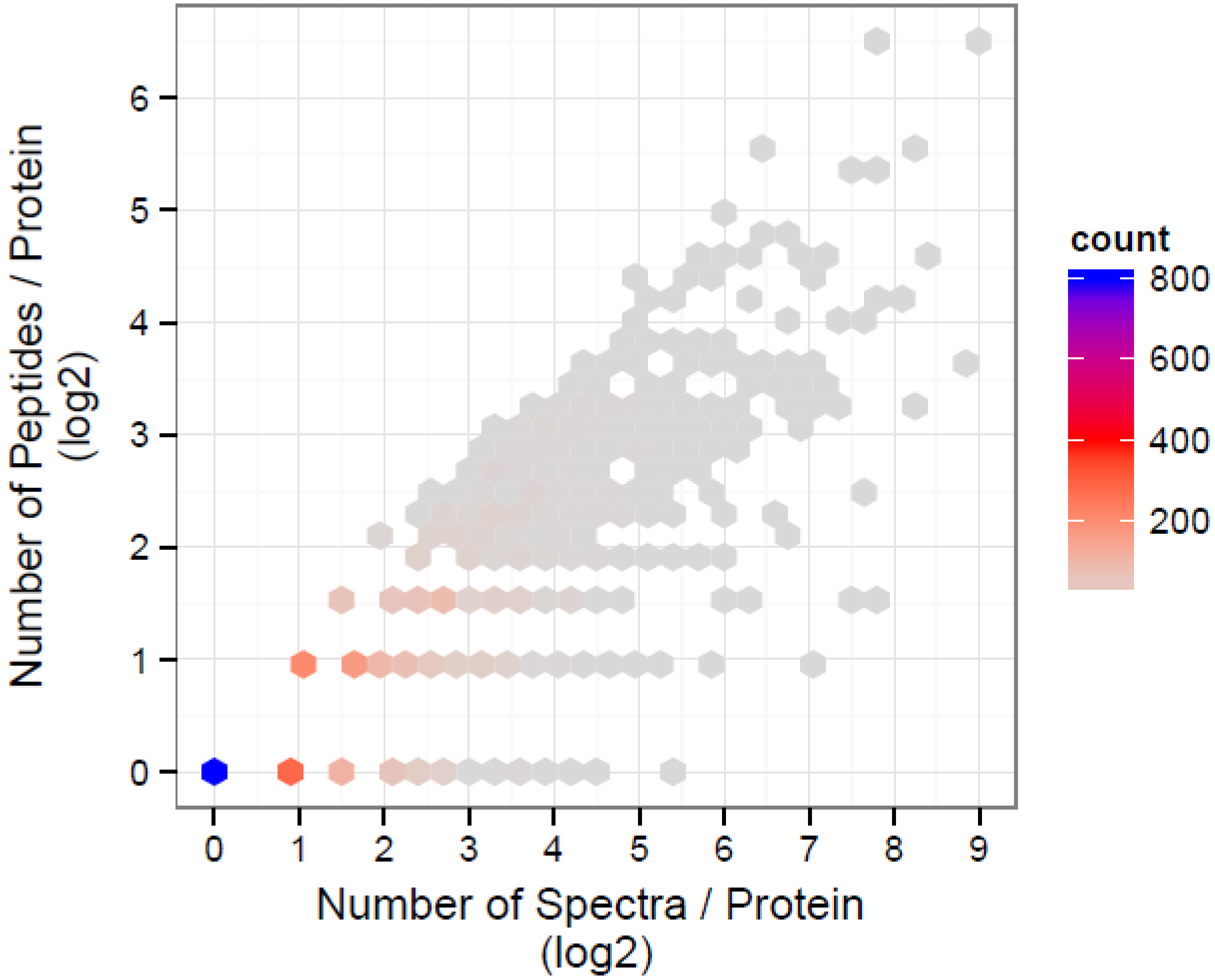
Figure S3. (a) Twenty proteins in the DEP dataset are annotated as lysosome-localized by the GO database. Among them, 15 proteins are also categorized as lysosomal by the hLGDB database. **(b)** Venn diagram showing the unique and overlaps in a subset of proteins from the DEP dataset that are assigned to 3 sub-endosomal compartments: the early endosome, the late endosome, and the recycling endosome.

Supplementary Figure S1 (a)



Supplementary Figure

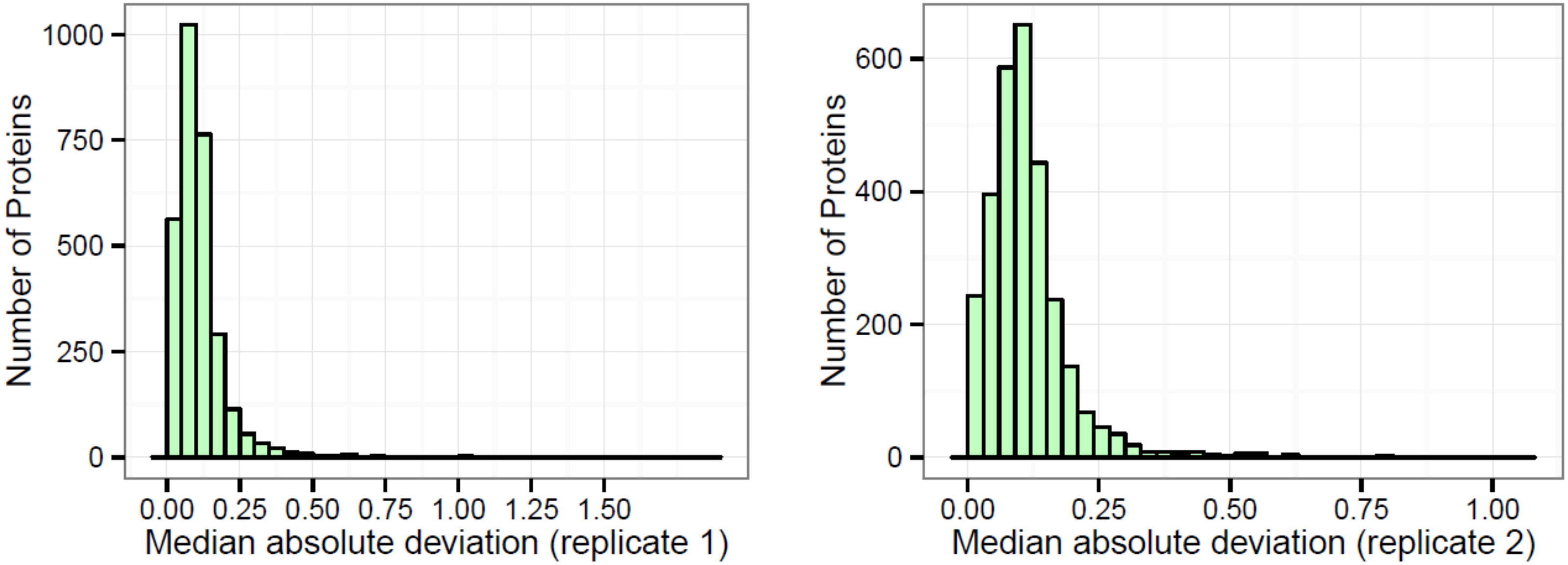
S1 (b)



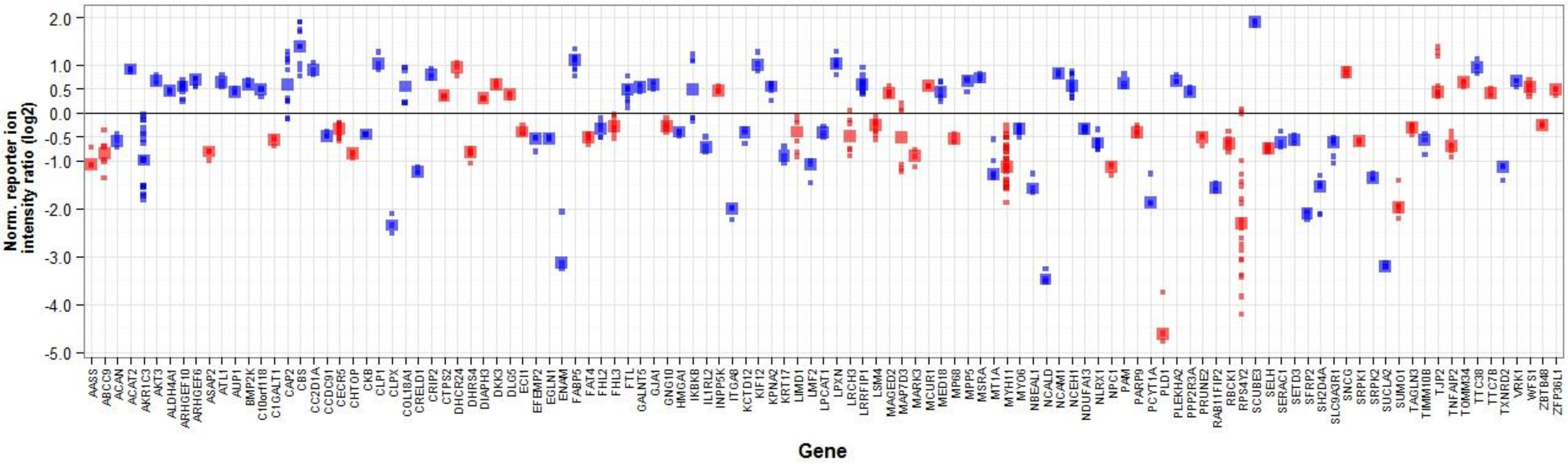
Supplementary Figure S1 (c)

No. of MS/MS spectra/ protein	No. of quantified Proteins (Percentage)	
	Experimental replicate 01	Experimental replicate 02
1	860 (29.5)	800 (27.4)
2	488 (16.8)	485 (16.6)
3	334 (11.5)	323 (11.0)
4	232 (8.0)	207 (7.1)
5	159 (5.5)	191 (6.5)
6 - 10	446 (15.3)	444 (15.2)
11 - 50	339 (11.6)	385 (13.2)
> 50	54 (1.9)	89 (3.0)

Supplementary Figure S1 (d)



Supplementary Figure S2



Supplementary Figure S3