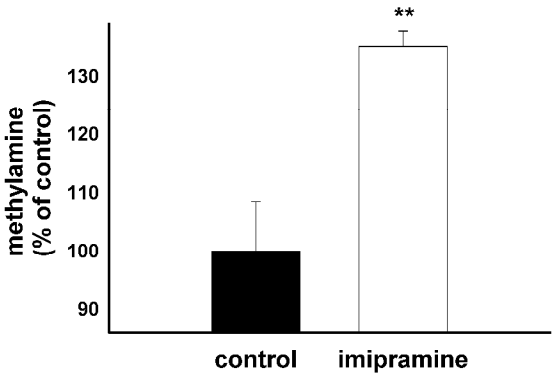
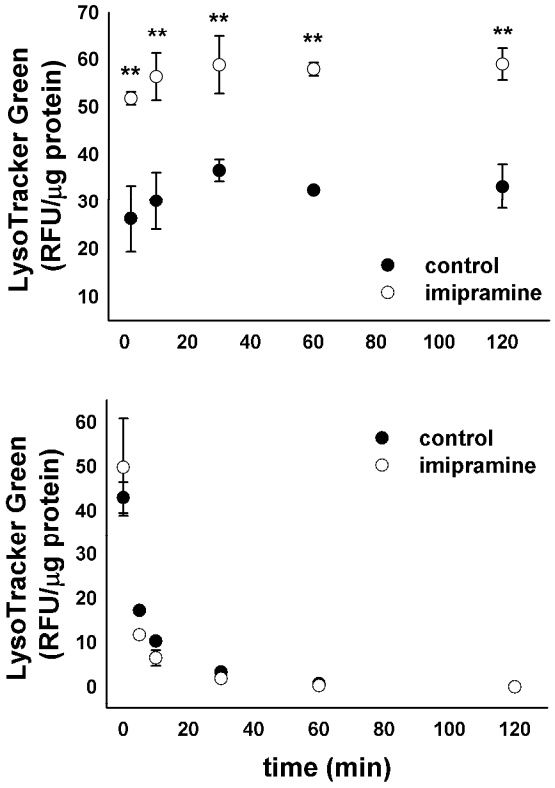
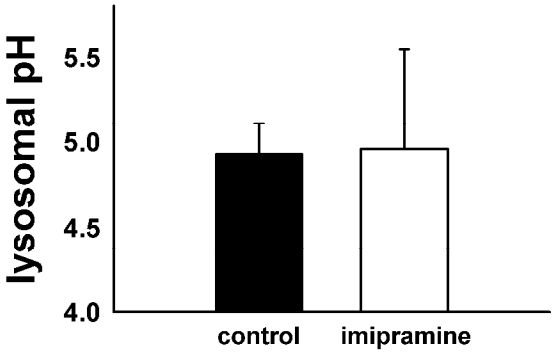
SUPPORTING INFORMATION



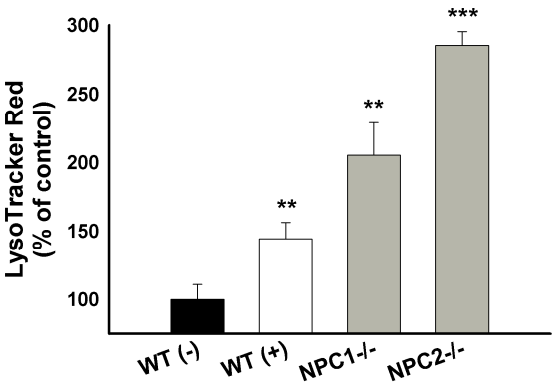
Supplemental Figure 1. Methylamine accumulation in MDA-1986 cells following a 24 h treatment with vehicle alone or 10 μM imipramine. Cellular accumulation of [^{14}C]methylamine as a percentage of vehicle-treated control cells is plotted as the mean ± S.D from three independent experimental evaluations (**, $p < .01$ by Student's t test).



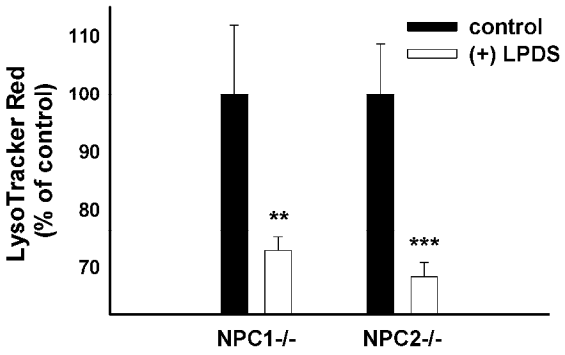
Supplemental Figure 2. LTG (A) uptake and (B) normalized release profile in MDA-1986 cells following a 48 h treatment with vehicle alone or 10 μM imipramine. Cellular LTG levels were measured in fluorescence units (RFU) and normalized to cellular protein and is represented as mean ± S.D from three independent experimental evaluations (**, $p < 0.01$ by Student's t test).



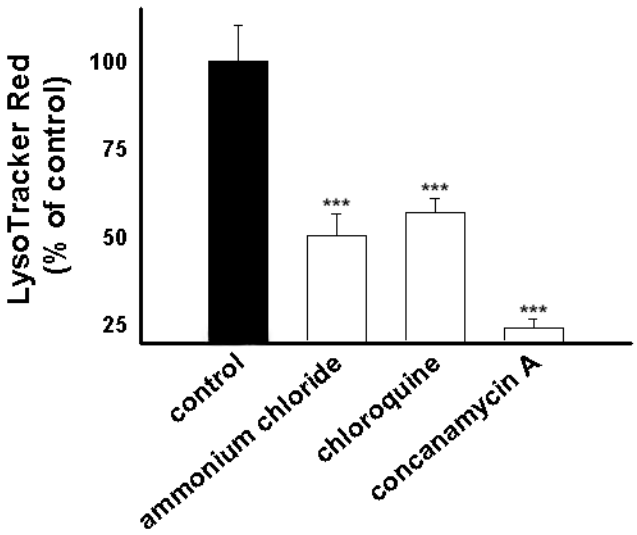
Supplemental Figure 3. Lysosomal pH in MDA-1986 cells following a 24 h treatment with vehicle alone or 10 μM imipramine. Lysosomal pH was evaluated by ratiometric measurements using a pH sensitive fluorescent probe targeted to lysosomes and is represented as mean ± S.D from at least three independent experimental evaluations.



Supplemental Figure 4. LTR accumulation in wild type (WT) human fibroblasts following a 24 h treatment with vehicle alone (WT (-)) or 10 μM imipramine (WT (+)), as well as, human fibroblasts from NPD patients with loss-of-function mutations in NPC1 (NPC1-/-) or (NPC2-/-). Cellular accumulation of LTR was normalized to the vehicle-treated WT cells and expressed as a percentage of control and is represented as mean ± S.D from three independent experimental evaluations (**, $p < 0.01$; ***, $p < 0.001$ by Student's t test).



Supplemental Figure 5. LTR accumulation in NPC disease fibroblasts with loss-of-function mutations in NPC1 (NPC1-/-) or NPC2 (NPC2-/-) that were grown under normal conditions (black bars) or with lipoprotein-depleted media (white bars). Cellular accumulation of LTR as a percentage of the amount accumulated under normal growth conditions for each cell line was determined and is represented as mean ± S.D from three independent experimental evaluations (**, $p < .01$; ***, $p < .001$ by Student's t test).



Supplemental Figure 6. LTR accumulation in MDA-1986 cells following a 2 h treatment with vehicle alone, 10 mM ammonium chloride, 30 μM chloroquine or 200nM concanamycin A. Cellular accumulation of LTR as a percentage of the vehicle-treated control cells is represented as mean ± S.D from at least three independent experimental evaluations (***, $p < .001$ by Student's t test).

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